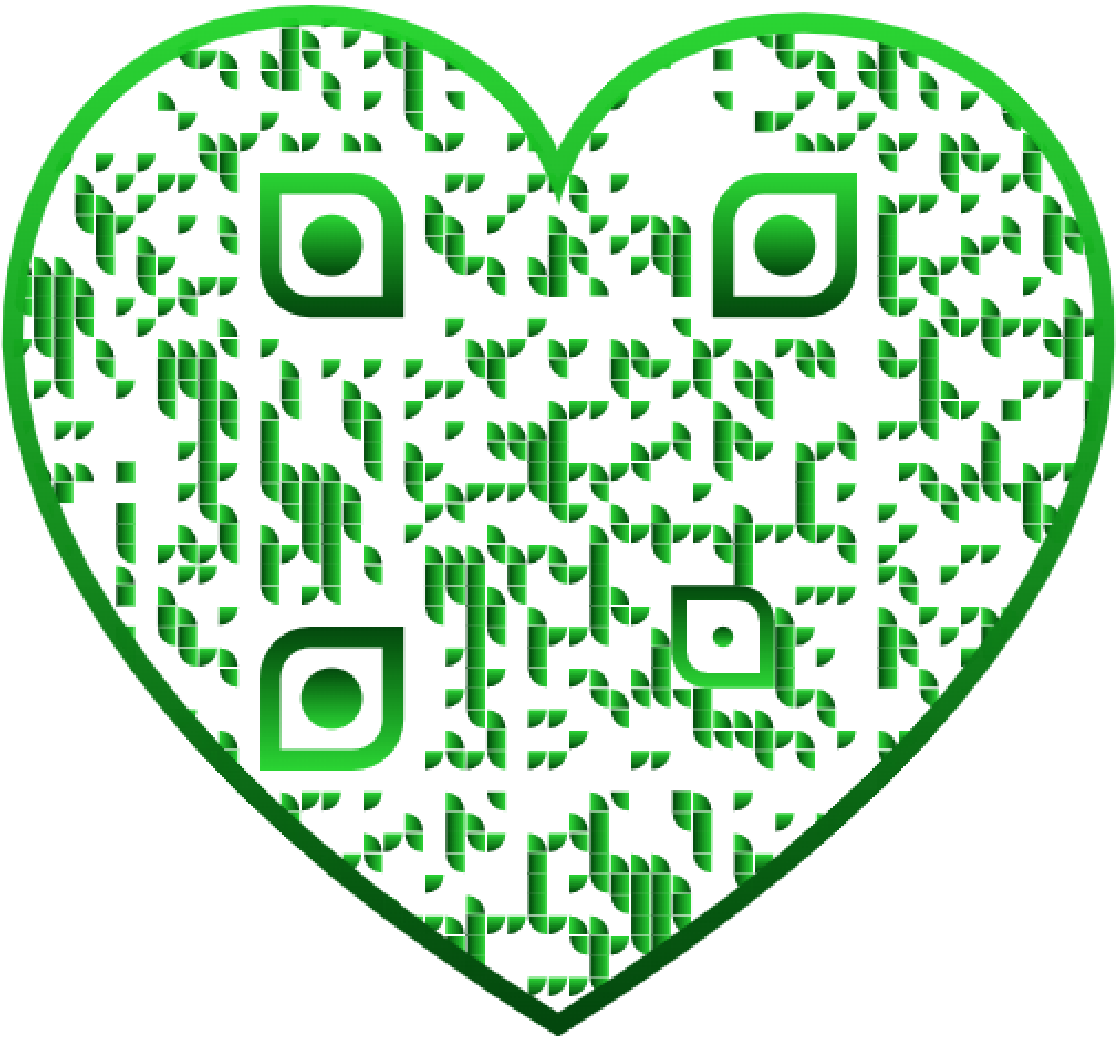
A SUMMARIZED GUIDE TO

HUMAN PHYSIOLOGY

CENTRAL NERVOUS SYSTEM

Uploaded By
Abdulrahman Zaghloul

MAGDI SABRY, MD



PREFACE

This new edition aims at summarizing vast subjects in human physiology into simplified and brief forms that can be easily revised. All essential points are discussed, and long subjects are abbreviated. However, the text remains indispensable not only for more knowledge but also for the importance of diagrams. Any suggestions will be welcomed and heartily appreciated. I hope this summarized guide will be a real help to medical students, specially in the short times that usually precede exams.

CONTENTS

Page

CHAPTER 1 : *The sensory receptors*.................................... 1

CHAPTER 2 : *The somatic sensations*.................................... 4

CHAPTER 3 : *Synapses & processing of signals in the CNS*...15

CHAPTER 4 : *Reflex actions*.. 21

CHAPTER 5 : *The stretch reflex and skeletal muscle tone*..... 25

CHAPTER 6 : *Some common lesions in the CNS*................ 35

CHAPTER 7 : *The thalamus*.. 40

CHAPTER 8 : *The hypothalamus*.. 42

CHAPTER 9 : *The basal ganglia*..45

CHAPTER 10 : *The cerebellum*.. 48

CHAPTER 11 : *The cerebral cortex*....................................... 52

CHAPTER 12 : *Posture and equilibrium*................................63

THE SENSORY RECEPTORS

These are special structures located at the peripheral ends of sensory (i.e. afferent) neurons. ***They inform the nervous system about changes that occur in both the external and internal environments of the body*** through *detecting such changes then transforming them into action potentials* (nerve impulses) that are conducted to the nervous system via the afferent neurons.

PROPERTIES OF THE SENSORY RECEPTORS

1. **Specificity :** Each receptor responds maximally to a specific form of energy called its ***adequate stimulus***, except pain receptors (nociceptors).

2. **Excitability :** This is the ability of the sensory receptors to respond to stimuli by producing a ***receptor (or generator) potential***. The latter is a state of *partial depolarization of the receptor* that occurs due to an increase in Na^+ influx secondary to activation of the Na^+ channels. It has the following ***properties*** :
   - a- *It does not obey the all or none law, so it can be graded.*
   - b- *It is not followed by an absolute refractory period, so it can be summated.*
   - c- *Its duration is long (about 5 milliseconds).*
   - d- *It is not blocked by local anaesthetic drugs.*
   - e- *It is conducted passively to the first node of Ranvier and results in a propagated action potential on reaching the threshold level.*

3. **Discharge of impulses :** This is determined by the intensity of the stimuli according to ***Weber-Fechner law***. This law states that "*the frequency of discharge from receptors is directly proportional to the logarithm of the intensity of the applied stimuli*".

4. **Adaptation :** *This is decline in the frequency of discharge from receptors on maintained stimulation by stimuli of constant strengths.* Its degree varies with the type of receptor, and the following are ***possible causes*** :

a- Gradual closure of the Na^+ channels in the receptors, which decreases the magnitude of the receptor potential.

b- Gradual decrease of the excitability of the first node of Ranvier.

c- Loss of the stimulus energy in the tissues with constant stimulation.

d- Accommodation of the afferent neuron to the receptor potential.

Adaptation of receptors is ***not due to their fatigue***, and the following table shows the *differences between both properties* :

	ADAPTATION	FATIGUE
Cause	Maintained stimulation	Previous stimulation
Mechanism	See above	Lactic acid accumulation
Effect of O_2 lack	No effect	Acceleration of fatigue
Onset and recovery	Rapid	Slow

CLASSIFICATION OF THE SENSORY RECEPTORS

The sensory receptors can be classified according to ***their degree of adaptation*** into **(a)** *Rapidly-adapting (= phasic) receptors* e.g. touch receptors **(b)** *Slowly-adapting (= tonic) receptors* e.g. the baroreceptors and pain receptors **(c)** *Moderately-adapting* receptors e.g. the smell and taste receptors and the thermoreceptors. They can also be classified according to ***their site*** into **(a)** *Exteroceptors* (the cutaneous and taste receptors as well as the ***teleceptors*** i.e. the receptors of vision, hearing and smell) **(b)** *Interoceptors* (the proprioceptors, visceroreceptors and hypothalamic receptors).

However, the sensory receptors are *preferably* classified according to ***their specificity*** into the following types :

1- Mechanoreceptors : These include :

- **a-** *Touch (tactile) receptors* e.g. Merkel's discs and Meissner's corpuscles
- **b-** *The baroreceptors* (e.g. those in the carotid sinus and aortic arch).
- **c-** *The proprioceptors* e.g. the muscle spindles and Golgi tendon organs.
- **d-** *The sound and vestibular receptors.*
- **e-** *The pressure receptors* in the skin & deep tissues (pacinian corpuscles)
- **f-** *The stretch receptors* (e.g. those in the right atrium & urinary bladder).

2- Thermoreceptors (which are special free nerve endings).

3- **Chemoreceptors** e.g. those in the carotid and aortic bodies, the taste and smell receptors and the hypothalamic glucoreceptors and osmoreceptors.

4- **Nociceptors** (the free naked nerve endings that perceive pain sensation).

5- **Electromagnetic receptors** (which are the rods and cones in the retinae of the eyes that perceive light sensation).

CODING OF SENSORY INFORMATION

This is the *discrimination (identification) of the modality (type), locality and intensity of the sensory information* by the nervous system.

1. **Modality discrimination** :The discrimination of the modality of a certain sensation depends on the *specificity of its receptors*. ***Muller's law*** states that "***Stimulation of a certain sensory pathway, no matter how or where, produces the sensation for which its receptors are specialized***"

2. **Locality discrimination** : The discrimination of the locality of a certain sensation depends on the *site of its receptors*. The ***law of projection*** states that "***Stimulation of a certain sensory pathway anywhere along its course produces a sensation that is projected to the locality of its receptors***".

3. **Intensity discrimination** : The discrimination of the intensity of a certain sensation depends on the following factors :
   - a- The number of the activated receptors.
   - b- The frequency of discharge from each activated receptor. The ***Weber Fechner law*** states that "***The frequency of discharge from receptors is directly proportional to the logarithm of the stimulus intensity***".
   - c- The state of nerve centres (e.g. the intensity is decreased if the nerve centres are depressed due to severe oxygen lack or hypoglycaemia).

CHAPTER 2

THE SOMATIC SENSATIONS

These include sensations from the ***skin and deep structures*** (except the viscera). Accordingly, they can be classified according ***to their site*** into **(a)** *Superficial, exteroceptive or cutaneous sensations* (pain, touch and temperature) **(b)** *Deep sensations* (proprioceptive, pressure and muscle sensations) **(c)** *Combined or synthetic senses* (vibration sense and stereognosis).

However, the somatic sensations are *preferably* classified according to ***the modality of the sensation*** into the following types :

1- **Mechanoreceptive sensations** : These include all tactile sensations (touch, pressure, vibration, itch and tickle sensations) as well as the muscle tension and proprioceptive sensations.

2- **Thermoreceptive sensations** (heat and cold sensations).

3- **Pain sensation**.

TOUCH SENSATION

There are 2 types of touch, ***crude and fine :***

(A) Crude touch : Its receptors are *free nerve endings & hair end organs.* Its afferent nerves are *A-delta nerve fibres*, and its central pathways are *the ventral spinothalamic tract & the posterior column tracts to some extent.*

(B) Fine touch : Its receptors are *Meissner's corpuscles & Merkel's discs.* Its afferent nerves are *A-beta nerve fibres*, and its central pathways are *the posterior column tracts (the gracile and cuneate tracts)*. It includes :

1- ***Tactile localization*** (topognosis).
2- ***Tactile discrimination*** (which is tested by ***Weber's compass***).
3- ***Stereognosis*** (recognition of objects without use of vision).
4- Sensation of the ***texture of materials***.

PRESSURE SENSATION

Its receptors are the *Pacinian corpuscles and Ruffini's endings*. Like touch, it may be fine (transmitted by the *gracile and cuneate tracts*) or crude (transmitted by the *ventral spinothalamic tract*). It is tested by the ability to differentiate between various weights that are placed in the hand while it is *supported on a table*.

MUSCLE TENSION SENSATION

Its receptors are the *Golgi tendon organs* and is transmitted by the *gracile and cuneate tracts*. It is produced by traction on the tendons, and is tested by the ability to differentiate between various weights *by lifting them*.

THE VIBRATION SENSE

It is tested by placing the *base of a vibrating tuning fork* on bony prominences. Its receptors are rapidly-adapting and include the *Meissner's corpuscles* (for vibrations up to 80 Hertz) and *Pacinian corpuscles* (for vibrations up to 700 Hertz). It is *closely related to proprioception* and is similarly transmitted by the *gracile and cuneate tracts*.

TICKLE AND ITCH SENSATIONS

Tickle results from mild tactile stimulation of the skin while itch results from skin irritation by either moving tactile stimuli or certain chemical substances e.g. histamine. Their receptors are *slowly-adapting free nerve endings* while their afferent nerves are *unmyelinated C nerve fibres* and they are transmitted by the *ventral spinothalamic tract*.

PROPRIOCEPTIVE (KINESTHETIC) SENSATIONS

These sensations arise from the muscles and joints, and are transmitted by the *gracile and cuneate tracts*. They include 2 types :

1-Sense of position (static proprioception) : Its receptors are slowly adapting and include the muscle spindles,Golgi tendon organs&Ruffini's endings.
2-Sense of movement (dynamic proprioception) : Its receptors are rapidly adapting and include the Pacinian corpuscles & Golgi tendon-like receptors.

THERMORECEPTIVE SENSATIONS

There are 2 types of thermoreceptors :

1. ***Internal*** (in the anterior hypothalamus, spinal cord & abdominal viscera).

2. ***External*** (under the skin) : These include the following receptors :

a- Warmth receptors : These are special *free nerve endings*. They transmit warmth by thin C nerve fibres and respond to temp. from 25 to 45-50 °C.

b- Cold receptors : These include *Krause's end bulbs* (which transmit cold by A-delta nerve fibres) and also free nerve endings to some extent. They are *4-10 times more than the warmth receptors* and respond to temperatures between 10 and 35 °C, and also ***briskly at 45-50 °C*** (which produces ***paradoxical cold sensation*** at this temperature).

The thermoreceptors ***detect the absolute temperature*** of the surrounding tissues. They are stimulated ***chemically*** (by changes in their metabolic rates) and they *adapt moderately*, mostly between 20 and 40 °C (the warmth receptors adapt more rapidly than the cold receptors). The thermal signals are ***transmitted along with pain by the lateral spinothalamic tract***.

PAIN SENSATION

Pain is an almost *non-adapting sensation* that is widely distributed in the body. The adequate stimuli that produce pain are ***not specific*** but they should be *noxious* (cause tissue damage). Its receptors are ***specific naked nerve endings*** (= nociceptors) that are 3 types (mechanical, thermal and chemical pain receptors). They require ***a high threshold of stimulation***, and they are ***stimulated chemically*** by certain substances released from damaged tissues e.g. bradykinin, histamine, serotonin and K^+ ions.

According to its site, pain may be ***cutaneous, deep or visceral***. However, it is commonly classified into ***fast (or immediate) & slow (or delayed) pain*** and the following table summarizes the differences between the 2 types :

	FAST PAIN (FP)	SLOW PAIN (SP)
Origin	skin	skin, deep tissues and viscera
Stimulus	mainly mechanical and thermal noxious stimuli	all noxious stimuli, specially chemical stimuli
Quality	pricking (sharp or acute)	burning (aching or chronic)
Perception	within 0.1 second	after one second or more
Duration	less than one second	many seconds to few minutes
Localization	well localized	diffuse (poorly localized)
Afferent nerves	A-delta nerve fibres	C nerve fibres
Carrying tract	neospinothalamic pathway	paleospinothalamic pathway
Centre in CNS	mainly cerebral cortex	mainly thalamus
Initiated reflexes	somatic protective reflexes	autonomic and somatic reflexes
Summation	absent	marked (becoming intolerable)
Depression	by pressure and hypoxia	by local anaesthetic drugs
Dissociation	can be dissociated from SP	can be dissociated from FP

Central perception of pain sensation

Pain is centrally transmitted by ***the lateral spinothalamic tract***. This tract also transmits *thermal and sexual sensations*, and it has 2 pathways :

1. **Paleospinothalamic pathway** : This transports *slow pain and thermal sensations specially heat*. The fibres that carry these sensations terminate at the *reticular formation and the periaqueductal gray area (PAG) as well as at the nonspecific thalamic nuclei (specially the intralaminar nuclei) and other subcortical centres at which the transported sensations are perceived*.

2. **Neospinothalamic pathway** : This transports *fast pain and thermal sensations specially cold*. The fibres that carry these sensations terminate at the *VPLN (ventral posterolateral nucleus of the thalamus)* from which other fibres arise and terminate at the *sensory areas of the cerebral cortex at which the transported sensations are perceived*.

Cutaneous pain

This may be *fast or slow* (see table above). It is *not referred to other areas* and shows the following reactions (effects) :

1. **Somatic reflexes** (specially *the protective withdrawal reflex*).
2. **Autonomic effects** (specially *sympathetic effects*).
3. **Emotional effects** (e.g. *restless, anxiety and crying*).
4. **Cutaneous hyperalgesia (tenderness)** :

This is pathological hypersensitivity to pain that often accompanies skin injuries, inflammation, burns and overexposure to sun rays. It is 2 types

*a- **Primary hyperalgesia** :* This occurs in the affected skin area and the surrounding red area of flare (V.D). In such areas the ***pain threshold is lowered*** due to sensitization of the pain receptors by substances released from damaged tissues,specially ***substance P***(which also produce V.D).These substances are released by ***antidromic signals as a result of a local axon reflex***

*b- **Secondary hyperalgesia** :* This occurs in the healthy skin area beyond that of primary hyperalgesia. In this area, *the pain threshold is not lowered but it is normal or even increased*. However, ***the evoked pain sensation is often prolonged and exaggerated***, and this is explained by the ***convergence facilitation mechanism***.

Deep pain

This originates from *muscles, joints, periosteum*, etc. It is initiated by trauma, fractures, inflammation, muscle spasm or ischaemia (= ***ischaemic pain***). The latter is due to accumulation of ***Lewis P factor*** (may be K^+) and common examples of it are *intermittent claudication and angina pectoris*.

Deep pain is *slow, diffuse, dull aching and may be referred* to other sites. It initiates *reflex contraction of the near muscles* and is commonly associated with *parasympathetic effects*.

Visceral pain

This is slow, diffuse, dull aching or spasmodic, and is ***often referred*** to other sites. It is commonly associated with sweating, nausea & vomiting as well as other parasympathetic effects, and it often causes *somatic reflexes* e.g. contraction of the anterior abdominal muscles (= *guarding rigidity*).

It is conveyed by *sympathetic nerves* (from the viscera lying between the thoracic and pelvic lines) and *parasympathetic nerves* (from the viscera lying beyond these lines), as well as by *certain somatic nerves* (e.g. the *phrenic nerves* that transmit pain from an inflamed gall bladder).

Its main causes are *visceral ischaemia, chemical stimuli* (e.g. HCl leaking from the stomach) and *mechanical stimuli* (e.g. overdistension of the hollow viscera, intestinal spasm and traction on the mesentery).

REFERRED (RADIATING) PAIN

This is pain that is felt away from its original site. It is most frequent with ***visceral pain***, and pain is referred to a somatic structure e.g. *pain of cholecystitis is usually referred to the tip of the right shoulder and cardiac pain to the left shoulder and inner side of the left arm*.

The structure in which pain originates and that to which pain is referred develop *from the same embryonic segment* and they are often at a considerable distance from each other due to *migration of organs during development*

Referred pain is explained by the *convergence projection mechanism*. The afferent nerves from the somatic structures (dermatomes, muscles and joints) and viscera that develop from the same embryonic segment converge on the same neurons of the spinothalamic tract, and since ***the brain is used to receive somatic stimuli only*** (and is almost unaware of the viscera), then *when a certain pathway carries pain signals from a diseased viscus, it projects the resulting pain sensation to the corresponding somatic structure*.

Protopathic and epicritic sensations

The protopathic (or primitive) sensations are those which are perceived at the ***thalamus***. They are crude sensations, and include *the gross movements of joints, crude pain and tactile sensations, and the extremes of temperature*. They are characterized by *being poorly-localized, require high threshold stimuli and are exaggerated (= thalamic hyperpathia)*.

On the other hand, the epicritic (or cortical) sensations are those which are perceived at the ***cerebral cortex***. They are fine sensations, and include e.g. *tactile localization and discrimination, stereognosis, fine pain and the fine grades of temperature*. They are characterized by *being well-localized, require low threshold stimuli and are not exaggerated*.

THE SENSORY (ASCENDING) TRACTS

There are 2 systems of ascending tracts :

(A) The anterolateral system : This consists of 2 tracts :

1- ***The ventral spinothalamic tract*** (which transmits *crude touch and pressure as well as the tickle and itch sensations*).

2- ***The lateral spinothalamic tract*** (which transmits *pain, thermal and sexual sensations*). It includes *2 separate pathways* (see fast and slow pain) :

a- **Paleospinothalamic pathway** (which transmits slow pain as well as thermal sensations specially heat).

b- **Neospinothalamic pathway** (which transmits fast pain as well as thermal sensations specially cold).

(B) The dorsal column lemniscal system : This consists of the ***gracile and cuneate tracts***. These tracts transport the following sensations :

1. The fine tactile sensations (*tactile localization & tactile discrimination*)
2. *Stereognosis and texture of material sensation.*
3. Fine pressure and muscle tension sensations.
4. The vibration sense.
5. The proprioceptive (kinesthetic) sensations.
6. Some crude touch and pressure sensations.

The *gracile tract transmits these sensations from the lower part of the body and lies medially in the dorsal column of the spinal cord while the cuneate tract transmits these sensations from the upper part of the body and lies laterally in the dorsal column.*

** There is an *accessory pathway to the gracile and cuneate tracts* called ***the spinocervical tract*** which conducts similar signals but at a faster rate.

The spinocerebellar tracts

These include 2 tracts (***dorsal and ventral***), and both conduct *proprioceptive signals to the cerebellum (subconsciously)* via the superior and inferior cerebellar peduncles.

SOMATIC SENSATIONS FROM THE HEAD

The somatic sensations ***from the face*** are transmitted by the 3 branches of the ***trigeminal nerve*** (the ophthalmic, maxillary and mandibular branches) while the somatic sensations ***from the back of head*** are transmitted by afferent nerve fibres in the ***second and third cervical nerves***.

HEADACHE

This is *referred pain at the head*. Its causes may be ***extra or intra-cranial***.

1- **Extracranial causes** :
   a- Eye diseases (e.g. glaucoma and hypermetropia).
   b- Diseases of the teeth and gums.
   c- Sinusitis.
   d- Otitis media and otitis externa.
   e- Emotions and tension (due to spasm of the head muscles).

2- **Intracranial causes** :
   a- Meningeal irritation (as occurs in *meningitis and brain tumours*).
   b- Lowering of the CSF pressure (e.g. *after a lumbar puncture*).
   c- Distension of the intracranial arteries (as occurs in fevers and hypertension as well as in *migraine*).

SYRINGOMYELIA

This is a slowly-progressive congenital disease in which there is an *abnormal overgrowth of neuroglial tissue associated with cavitation around the central canal of the spinal cord.* This causes the following manifestations

1. ***Dissociated sensory loss :*** There is *bilateral loss of pain and temperature sensations at the level of the lesion* (due to damage of the lateral

spinothalamic tracts while crossing in front of the central canal) while the *fine tactile and proprioceptive sensations remain intact* (because the gracile and cuneate tracts in the dorsal columns of the spinal cord are not affected). This commonly takes ***a jacket distribution*** because the lesion usually occurs in the *lower cervical and upper thoracic segments of the spinal cord.*

2. Bilateral paralysis at the level of the lesion : This is of *the lower motor neuron type due to damage of the anterior horn cells.*

3. Horner's syndrome may occur (due to damage of the lateral horn cells).

4. Paraplegia may occur (if the pyramidal tracts are injured).

5. Paralysis of some cranial nerves (in cases of syringobulbia).

TABES DORSALIS

This is a disease that occurs in the late stage of ***neurosyphilis*** as a result of *inflammation of the dorsal nerve roots* (which is commonly bilateral at the lower thoracic and lumbosacral regions of the spinal cord).This causes the following manifestations :

(A) Early manifestations

1. Attacks of very sharp pain (= *lightning pain*) due to irritation of the pain-conducting afferent nerve fibres.

2. Degeneration of the gracile and cuneate tracts leading to tabes (i.e. atrophy) of the dorsal column of the spinal cord (due to damage of the thick A fibres as a result of *compression*). This leads to the following symptoms :

a- ***Loss of the fine tactile sensations as well as the vibration sense.***

b- ***Sensory ataxia :*** This occurs due to loss of both the conscious proprioceptive sensations (the kinesthetic sensations) as well as the nonconscious proprioceptive information to the cerebellum. It is characterized by ***walking at a broad base with a stamping gait as well as a positive Romberg's sign***.

(B) Late manifestations

1. Loss of all sensations as well as all reflexes in the regions innervated by the affected dorsal roots, including **(a)** Superficial reflexes e.g the withdrawal reflex (which leads to skin injury and ulceration) **(b)** Deep reflexes e.g. the stretch reflex (which results in loss of the muscle tone and tendon jerks) **(c)** Visceral reflexes e.g. the micturition reflex (which results in urine retention with overflow).

2. ***Argyll-Robertson pupil*** : This may occur in the late stage of the disease *due to damage of the pretectal area in the midbrain* (see special senses).

SUBACUTE COMBINED DEGENERATION

This is a slowly-progressive disease due to ***deficiency of vitamin B_{12}***. It is characterized by *bilateral degeneration of the dorsal & lateral columns of the spinal cord (specially in the lumbosacral region) as well as by poly-neuropathy*. These lesions lead to the following manifestations *mainly in the lower limbs* :

1. ***Loss of the conscious proprioceptive (kinesthetic) sensations and sensory ataxia*** (due to degeneration of the gracile and cuneate tracts).
2. ***Paraplegia*** (as a result of degeneration of the pyramidal tracts).
3. ***Paraesthesia*** (secondary to polyneuropathy).

PAIN SUPPRESSION (= PREVENTION) IN THE CNS

This was explained by ***the gate theory*** but recently it was found to be produced by a special system called the ***"pain control analgesia system"***.

THE GATE THEORY OF PAIN CONTROL

This theory assumes that the various relay stations in the pain pathway in the CNS act as gates *that can be closed*, thus preventing transmission of pain signals to the high centres. These gates are located in the *substantia gelatinosa of Rolandi (spinal gate), the reticular formation and the thalamus*.

At the spinal gate, pain transmission can be blocked by signals that produce ***presynaptic inhibition of the pain afferent fibres***. These signals are derived from either **(a)** *Collaterals from the thick myelinated fibres in the dorsal column* **(b)** *Descending fibres from certain higher centres called the corticofugal or centrifugal fibres* (which can also prevent pain transmission at the thalamic and reticular gates).

THE PAIN CONTROL ANALGESIA SYSTEM

This system includes mainly the following structures :

1. *The periventriculr nuclei (PVN) in the hypothalamus.*
2. *The periaqueductal gray area (PAG) in the midbrain.*
3. *The raphe magnus nucleus (RMN) in the medulla oblongata.*
4. *The pain inhibitory complex (PIC) in the dorsal horns of spinal cord.*
5. *The limbic association areas in the cerebral cortex.*

The principal mediators in this system are the ***opioid peptides***, specially *endorphins and enkephalins*, and it ***blocks pain transmission mainly by exciting the (PIC)***.The latter is formed of multiple short enkephalinergic interneurons that are located in relation to the pain afferent nerve terminals. These terminals contain ***opiate receptors***, and when the (PIC) is excited, the released enkephalin binds to such receptors.This prevents the release of substance P from the pain nerve terminals,resulting in ***presynaptic inhibition of pain transmission***.

Pain inhibition by this mechanism occurs through 2 pathways :

1. Spinal inhibition (peripheral pathway of pain inhibition)

Collaterals from the thick A-beta fibres that transmit mechanoreceptive sensations *directly stimulate the (PIC)*. This explains pain relief by counter-irritants, mechanical stimuli (e.g. rubbing of the skin) and *acupuncture*.

2. Supraspinal inhibition (central pathway of pain inhibition)

Excitation of the hypothalamic (PVN) or certain areas in the cerebral cor-tex (see above) depresses pain. This is responsible for ***stress analgesia***, and occurs as follows :

a- The hypothalamic&cortical fibres release ***endorphin*** that excites the PAG
b- The (PAG) projects ***enkephalinergic neurons*** that stimulates the (RMN).
c- The (RMN) projects ***serotonergic neurons*** that activate the (PIC).

** *It is probable that the analgesia system also inhibits pain transmission at the thalamic intralaminar nuclei and the reticular nuclei in the brain stem by the released opioid peptides.*

CHAPTER 3

SYNAPSES AND PROCESSING OF SIGNALS IN THE CNS

TYPES OF SYNAPSES & MECHANISM OF IMPULSE TRANSMISSION

1.**Chemical synapses** : These are the ***majority***. Stimulation of the presynaptic neurons causes release of ***chemical transmitters*** from their endings (= synaptic knobs) that affect the excitability of the postsynaptic neurons.

Depolarization of the synaptic knobs leads to opening of *voltage-gated Ca^{++} channels*.This allows ***Ca^{++}influx*** into the knobs and Ca^{++} leads to movement of the transmitter vesicles toward the knob's membranes then their rupture and release of the transmitter into the synaptic clefts by ***exocytosis***.

The released transmitter then binds to ***specific synaptic receptors***. This triggers either opening or closure of certain ***ligand-activated ion channels***, which results in electric changes that lead to a state of either excitation or inhibition at the synapse depending on the nature of the released transmitter.

2.**Electrotonic synapses** : ***Gap junctions*** form between presynaptic & postsynaptic neurons. These gaps constitute ***low-resistance bridges*** that allow *direct transmission of depolarization waves from one neuron to the other*.

3.**Conjoint synapses** : These are ***very rare*** in the CNS, and the transmission of impulses across them occurs ***both chemically and electrically***.

TYPES OF SYNAPTIC RECEPTORS

1. **Presynaptic receptors** : These *usually cause inhibition of the release of chemical transmitters* e.g. the ***alpha-2 receptors at the noradrenergic presynaptic nerve endings*** that are excited by the liberated noradrenaline but inhibit its further release.

2. **Postsynaptic receptors**:Excitation of these receptors causes postsynaptic potentials. There are often several receptors for each neurotransmitter e.g. :

a- The acetylcholine receptors (5 muscarinic and 2 nicotinic receptors).
b- The adrenergic receptors (2 alpha and 3 beta receptors).
c- The dopamine (D) receptors (5 receptors).
d- The histamine (H) receptors (3 receptors).
e- The GABA receptors (2 receptors).
f- The serotonin receptors (7 receptors).

TYPES OF POSTSYNAPTIC POTENTIALS (PSPs)

1. Excitatory postsynaptic potential (EPSP) :

This is a state of ***transient depolarization*** in the postsynaptic membrane. It is produced by excitatory transmitters e.g. ***acetylcholine*** (through ***increasing Na^+ influx***) and ***noradrenaline*** (through ***decreasing K+ efflux***).

2. Inhibitory postsynaptic potential (IPSP) :

This is a state of ***transient hyperpolarization*** in the postsynaptic membrane. It is produced by certain inhibitory transmitters specially ***glycine*** (which acts mainly through ***increasing Cl^- influx***).

** During rest, there is little activity in both the excitatory and inhibitory synapses, producing ***miniature EPSP and miniature IPSP respectively***.

SUMMATION OF POSTSYNAPTIC POTENTIALS (PSPs)

A single PSP is normally *very small and fails to effect the activity of the postsynaptic neuron*. However, it is ***not an all or none response and can be summated*** (thus affecting postsynaptic activity) by the following 2 ways :

1. Spatial summation : This is more common in the CNS.It occurs when many PSPs are produced *at the same time as a result of simultaneous excitation of several presynaptic neurons*.

2. Temporal summation : This is less common and it occurs when many PSPs are produced *successively as a result of repeated excitation of a single presynaptic neuron*, provided the intervals between the successive impulses are *less than 15 milliseconds* (the time after which a single PSP decays).

** When both excitatory and inhibitory presynaptic neurons converge on a postsynaptic neuron, their *simultaneous stimulation* produces an effect that depends on which of them is predominant. If the EPSPs predominate, a **central excitatory state** is produced (in which the postsynaptic membrane is depolarized) while if the IPSPs predominate, a **central inhibitory state** is produced (in which the postsynaptic membrane is hyperpolarized).

MECHANISMS OF SYNAPTIC INHIBITION

1. **Postsynaptic (direct) inhibition** :

In this case, the terminal knobs of the inhibitory neurons lie ***in direct contact with the postsynaptic neuron***, and the transmitter (which is mostly ***glycine***) leads to synaptic inhibition by producing IPSP (see above).

2. **Presynaptic inhibition** :

In this case, the terminal knobs of the inhibitory neurons ***terminate on the excitatory nerve endings*** and the released transmitter (*enkephalin in the dorsal horns and GABA in other areas*) ***decreases Ca^{++} influx into these nerve endings, thus the liberation of the excitatory transmitter is decreased, which leads to reduction of postneuronal excitation***.

PROPERTIES OF SYNAPTIC TRANSMISSION

1. **One way conduction (forward conduction)** : In synapses, the impulses are conducted *only from presynaptic to postsynaptic neurons*.

2. **Delayed conduction (synaptic delay)** : The conduction of impulses across *a single synapse* is normally delayed about *0.5 millisecond*.

3. **Synaptic fatigue** : This usually occurs after repetitive stimulation of the presynaptic neurons, mainly due to *exhaustion of the neurotransmitter*, and it results in *slowing or block of impulse transmission across synapses*.

4. **Synaptic afterdischarge** : This is continued discharge of the postsynaptic neurons after the initial excitatory signals stop. Its duration varies with the excitatory transmitter, and it can be prolonged if its inactivation is delayed.

5. **Summation of PSPs** : This may be *spatial or temporal* (see above).

6. **High sensitivity to the following** :

a- pH : Alkalosis increases while acidosis decreases synaptic transmission

b- Blood oxygen level : Hypoxia decreases synaptic transmission.

c- Drugs and chemicals : Synaptic transmission is *increased* by caffeine, strychnine, tetanus toxin and picrotoxin, while it is *decreased* by anaesthetic hypnotic, anti-anxiety and tranquilizer drugs as well as by alcohol.

7. **Synaptic plasticity** : This is modification of the strength of synaptic transmission. Such modifications may be ***short-term or long-term*** and are related to development of ***memory and learning***. They include the following :

(a) Synaptic potentiation : A good example of this is the phenomenon of ***posttetanic potentiation***. This is short-term production of increased PSPs in response to stimulation after applying a brief tetanizing train of stimuli to the presynaptic neurons, and is due to *more release of the neurotransmitter*. Long-term potentiation (LTP) can also occur.

(b) Synaptic depression : A good example of this is the phenomenon of ***habituation*** This is gradual disappearance of the response to a benign stimulus if it is repeated over and over It is due to *less release of the neurotransmitter*, and it may be short-term or prolonged if exposure to the stimulus is repeated many times. Long-term depression (LTD) can also occur.

(c) Synaptic sensitization : This is augmentation of the postsynaptic response to a *previously-habituated presynaptic stimulus*, if it is paired once (or more times) with a noxious stimulus. Such effect may be short-term or long-term (if reinforced by additional pairings of the noxious and initial stimuli).

THE SYNAPTIC TRANSMITTERS

These exceed 40 in the CNS, and they can be classified into 2 types :

(A) Small molecule rapidly acting transmitters :

1. ***Acetylcholine***.
2. ***Amines*** (epinephrine, norepinephrine, dopamine, serotonin & histamine)
3. ***Amino acids*** e.g. *glutamic and aspartic acids* (excitatory transmitters) and *glycine and GABA* (inhibitory transmitters).

(B) Large molecule slowly acting transmitters :

These are ***polypeptides***, and include the following :

1. ***Opioid peptides*** (specially *enkephalins and endorphins*).
2. ***Non-opioid peptides*** (*hypophyseotropic hormones, some GIT hormones, ATP, adenosine, substance P, angiotensin II, neurotensin and ANP*).

Acetylcholine : This is an *excitatory* transmitter that is essential for *intellectual functions (memory & learning), consciousness and motor functions*.

Epinephrine and norepinephrine : This is an *excitatory* transmitter that is essential for *improvement of the mood.*

Dopamine : This is an *inhibitory* transmitter that is present mainly in the *basal ganglia*, and its deficiency leads to a disease called *Parkinsonism*.

GABA (Gamma AminoButyric Acid) : This is an *inhibitory* transmitter that is concerned with *presynaptic inhibition*.It requires *vitamin B_6 as a cofactor*. Its effect is *antagonized by picrotoxin* and *facilitated by alcohol and valium*.

Glycine : This is an *inhibitory* transmitter that is concerned with *postsynaptic inhibition*, and its effect is *antagonized by strychnine & the tetanus toxin*.

Substance P : This substance is released by the neurons that *mediate pain* as well as the antidromic neurons that produce *flare & primary hyperalgesia*

PROCESSING OF SIGNALS IN THE CNS

When an input signal enters a pool of neurons, it is ***processed to produce an appropriate output signal***. The input signals do not affect all pools equally (= ***fractionation of pools***), and ***through the interneurons***, they may be ***diverged, converged, prolonged, shortened or sharpened***.

The neurons affected by an excitatory input neuron constitute ***the excitation field of that neuron***. The central neurons in this field discharge (so the central zone is called the ***firing or discharge zone***) while the ***peripheral neurons are only facilitated*** (so the peripheral zone in an excitation field is often called the ***facilitated zone or subliminal fringe***).

Prolongation of signals in neuronal pools (afterdischarge)

This is prolonged output discharge after stoppage of the input signal. It is due to either : **(a) Synaptic afterdischarge** (page 17) **(b) Interneuronal barrages** (= *parallel or reverberatory circuits of interneurons that re-excite the output neurons for several milliseconds after the input signal stops*).

Shortening of signals in neuronal pools

This can occur by one of the following 2 mechanisms :

1. **Negative feedback (recurrent) inhibition** : A recurrent collateral from the excitatory neuron stimulates an inhibitory interneuron, which turns back and inhibits the same excitatory neuron. A good example of this mechanism is is the ***Renshaw cells*** (which are ***inhibitory interneurons present in the anterior horns of gray matter of the spinal cord***).

2. **Negative feedforward inhibition** : A collateral from the excitatory neuron stimulates an inhibitory interneuron which proceeds and inhibits the discharge from the output neuron. This specially occurs in the ***cerebellum***.

Sharpening of signals in neuronal pools

This occurs through *inhibiting the activity of the nearby neurons in the pool* , which can occur by one of the following 2 mechanisms :

1. **Lateral inhibition** : A good example of this mechanism is also the ***Renshaw cells*** (see above). This inhibitory interneuron (which is stimulated by the recurrent collateral from the excitatory neuron) *does not only inhibit the same excitatory neuron but also inhibits the activity of the surrounding neurons*, which helps to focus (or sharpen) the activity of the output neuron.

2. **Reciprocal inhibition** : This occurs specially *during spinal reflexes* via certain circuits e.g. during the stretch reflex, the input signals from the stretched muscle directly stimulate the motor neurons that supply this muscle, and at the same time stimulate certain inhibitory interneurons called ***golgi bottle neurons***. The latter inhibit the activity of the motor neurons that supply the antagonistic muscles, so the signals discharged to the stretched muscle are sharpened, leading to an optimal and unopposed contraction.

REFLEX ACTIONS

THE HUMAN REFLEXES

These can be classified as follows :

(A) Peripheral reflexes

1- **Local axon reflexes** e.g. that producing flare of the triple response.
2- **Local enteric reflexes** e.g. that producing peristalsis in the GIT.
3- **Ganglionic reflexes** e.g. the enterogastric reflex (refer to digestion).

(B) Central reflexes

(1) **Conditioned reflexes** (the *acquired reflexes* that develop by learning)
(2) **Unconditioned reflexes** : These are *inborn (inherent)* and include :
  1- Hypothalamic reflexes e.g. those regulating body water and temp.
  2- Midbrain reflexes (mediate some postural and visual reflexes).
  3- Medullary reflexes (cardiovascular,digestive &respiratory reflexes)
  4- Spinal reflexes : These include the following reflexes :
    a. Visceral reflexes e.g the micturition and defecation reflexes.
    b. Deep reflexes e.g. the stretch reflex and Philipson's reflex (page 30) as well as the various stepping reflexes.
    c. Superficial (cutaneous) reflexes : These include the following :

*1- **The plantar reflex*** (the centre of which is mainly the first sacral segment)
*2- **The abdominal reflexes*** (the centre of which is 7-12 thoracic segments).
*3- **The cremasteric reflex*** (the centre of which is 1 and 2 lumbar segments).
*4- **The withdrawal (or flexor) reflex*** (which is initiated by noxious stimuli).
*5- **The crossed extensor reflex*** (which is a *supportive in function*).
*6- **The anal reflex*** (the centre of which is 3 and 4 sacral segments).
*7- **The positive supporting reflex*** (a supporting reflex, the centre of which extends from the first lumbar to the first sacral segments).
*8- **The scratch reflex*** (which is initiated by the itch sensation).

**** The corneal reflex is also a superficial (but not cutaneous) reflex.**

THE PROPERTIES OF REFLEX ACTIONS

All reflex actions in the body are polysynaptic except the stretch reflex (see chapter 5). The following are the ***properties of polysynaptic reflexes*** :

(1) **Forward direction (conduction)** : Impulses in reflex actions are conducted *only from the afferent to the efferent neurons.*

(2) **Localization (local sign)** : The locality and pattern of the response in a reflex are determined by the site of the stimulus.

(3) **Central delay** : This is the time of conduction of impulses in the CNS. It is due to *synaptic delay* (page 17), and is thus proportionate to the number of synapses in the reflex arc.

(4) **Summation** : This may be *spatial or temporal* (page 16).

(5) **Fatigue** : This is due to *synaptic fatigue* (page 17), and it may be followed by block (disappearance of the response).

(6) **Central inhibition and central facilitation** :In most reflexes facilitation occurs in some pools and inhibition occurs in other pools e.g. in the lateral inhibition (page 20), which is important to obtain optimum responses.

(7) **Reciprocal innervation** : This is simultaneous stimulation of the motor neurons that supply certain muscles and inhibition of the motor neurons that supply their antagonists. ***It occurs in all reflexes except the positive supporting reaction*** (page21)in which the pressure on the feet during standing causes *contraction of both flexors & extensors of the lower limbs.*

(8) **Irradiation** : This is spread of an input signal in the CNS from one neuronal pool to another by *divergence*. Its intensity (and consequently, the magnitude of response) is *proportionate to the intensity of the stimulus.*

(9) **Occlusion** : Stimulation of 2 near afferent neurons *simultaneously* produces a *smaller response* than the algebraic sum of the responses obtained

when each afferent is stimulated separately. This is due to *overlap of the discharge zones of both afferent neurons.*

(10) **Subliminal fringe summation** : This is the opposite of occlusion. Stimulation of 2 near afferent neurons *simultaneously* produces a *greater response* than the algebraic sum of the responses obtained when each afferent is stimulated separately. This is due to *overlap of the subliminal fringe zones of both afferent neurons* (the nerve cells in which are *only facilitated when each afferent is stimulated separately, but they discharge when both afferent neurons are simultaneously stimulated*).

(11) **Recruitment and afterdischarge** : Recruitment is the progressive activation of motor neuron pools while afterdischarge is the continued discharge from these pools after the input signals stop. These properties are mainly due to ***interneuronal barrages*** (page19) and are studied by comparing ***reflex tetanus and motor tetanus***. They are *evident in reflex tetanus as shown in the following table* :

	REFLEX TETANUS	MOTOR TETANUS
Production	Stim. of afferent nerve	Stim. of efferent nerve
Latent period	Long	Short
Muscle contraction	Rises gradually (recruitment)	Rises sharply (rapidly)
Maximal tension	Lower than motor tetanus	Higher than reflex tetanus
Fatigue	Rapid (due to synaptic fatigue)	Slow
Muscle relaxation	Gradual (due to afterdischarge)	Sudden

(12) **Rebound** :This is augmentation of a reflex after it has been temporarily inhibited. It is probably due to accumulation of central excitatory states in the reflex arc during the period of inhibition.

(13) **Successive spinal induction** : This is facilitation of a reflex by another reflex. It occurs when successive reflexes are produced, and it may be ***positive*** (when the reflexes are synergistic e.g. successive scratch reflexes initiated by a moving flea) or ***negative*** (when the reflexes are antagonistic e.g. successive flexion and extension of a limb during walking).

PROPERTIES OF THE WITHDRAWAL (FLEXOR) REFLEX

This is a ***protective prepotent superficial spinal reflex*** (i.e. it inhibits other reflexes occurring at the same time). It is a ***typical polysynaptic reflex*** that is initiated by noxious stimuli, and it has the following properties :

1. ***Precise localization.***
2. ***Long central delay.***
3. ***Irradiation.***
4. ***Reciprocal innervation.***
5. ***Recruitment.***
6. ***Afterdischarge.***
7. ***Occlusion.***
8. ***Summation of EPSPs.***
9. ***Fractionation of motor neuron pools (page 19).***

PROPERTIES OF THE CROSSED EXTENSOR REFLEX

This is reflex extension of a limb during flexion of the other limb as a result of a withdrawal reflex.It is ***supportive*** in function, and its arc contains *more interneuronal circuits than those in the withdrawal reflex* because signals are transported to the opposite side of the spinal cord. It has ***the same properties of the withdrawal reflex***, but in comparison, ***it has a more prolnoged central delay (so its latent period is longer) as well as a more prolonged afterdischarge***.

PROPERTIES OF THE SCRATCH REFLEX

This is a superficial spinal reflex that is initiated by ***multiple linear tactile stimuli*** (e.g. those produced by a crawling insect across the skin) or by ***a moving weak faradic current***, and it has the following properties :

1. ***Precise localization*** (so that the scratching limb goes to the exact point of irritation).
2. ***Reciprocal innervation*** (so that the scratching to and fro movements can be performed properly).
3. ***Positive successive spinal induction*** (so the scratching movements become progressively stronger).

THE STRETCH REFLEX AND SKELETAL MUSCLE TONE

The stretch reflex is a reflex contraction of skeletal muscles in response to passive stretch. Its receptors are ***the muscle spindles***, so it is also called the ***muscle spindle reflex (MSR)***. Its centre is the large *alpha motor neurons* in the anterior horns of the spinal cord, and its reflex arc consists of only afferent and efferent neurons (*it contains no interneurons*), so it is a ***monosynaptic reflex*** (probably the only in the body).

The muscle spindle : This receptor consists of several ***intrafusal muscle fibres***, which are 2 types : ***nuclear bag and nuclear chain fibres***. Only the ***peripheral parts of these fibres are contractile***, and they are supplied by 2 types of ***gamma efferent neurons*** (see below)..

When a skeletal muscle is passively stretched or the peripheral parts of the muscle spindles contract (by activation of the gamma efferent neurons), the central non-contractile parts of the muscle spindles are stretched and signals are discharged from these parts by *2 types of sensory or afferent neurons* :

1. Type Ia nerve fibres : These are A alpha fibres that arise from *annulo-spiral (primary) endings* in the central parts of *both types of intrafusal fibres*

2. Type II nerve fibres : These are A beta fibres that arise from *flowerspray (secondary) endings* in the central parts of *the nuclear chain fibres only*.

THE "H" (Hoffmann's) reflex : This is ***an induced stretch reflex*** that is obtained by electric stimulation of the Ia afferent fibres from a muscle).

Function of the muscle spindles : The muscle spindles constitute ***a feedback mechanism that maintains the muscle length constant***. Elongation of a muscle (by stretch) excites the muscle spindles, leading to contraction of the muscle and its shortening. Conversely, muscle shortening decreases the discharge from the muscle spindles, leading to muscle relaxa-tion and its elongation (the latter response is called ***negative stretch reflex***).

Responses of the muscle spindles to stretch

1. ***Dynamic response* :** This occurs while the muscle length is increasing, informing the CNS about the *rate of change of muscle length*. Its receptors are the *primary endings*, so it is a *rapidly-adapting response*..
2. ***Static response* :** This occurs throughout the period of stretch, informing the CNS about *changes in the muscle length*. Its receptors are mainly the *secondary endings*, so it is a *slowly-adapting response*.

TYPES OF THE STRETCH REFLEX

1. *Dynamic stretch reflex* : This is initiated by sudden stretch of the muscle, and the response is a brief strong contraction (as occurs in ***tendon jerks***). It is produced by the ***dynamic response*** of the muscle spindles (see above).
2. *Static stretch reflex* : This is initiated by steady stretch of the muscle, and the response is a maintained contraction (as occurs in ***skeletal muscle tone)*** and is produced by the ***static response*** of the muscle spindles (see above).
3. *Negative stretch reflex* : This occurs by muscle shortening (see above).
4. *Inverse stretch reflex* : This is discussed in detail later (page 29).
5. *Cerebellar stretch reflex* : Refer to the cerebellum (chapter 10).

The following table shows the differences between the static and dynamic stretch reflexes :

	DYNAMIC STRETCH R.	STATIC STRETCH R.
Stimulus	Sudden stretch	Maintained stretch
Afferent fibres	Type Ia fibres	Type II fibres
Response	Brisk contraction and rapid relaxation	Maintained smooth contractio
Function	Clinical significance only	Production of muscle tone
Fatiguability	Rapid	Slow
Adaptation	Rapid	Slow
Enhancement	Enhanced by Jendrassik's maneuver	Not affected by any maneuver
Existence	Not normally existent (elicited only clinically by the hammer)	Exists normally in all muscles (specially antigravity muscles)

FUNCTIONS OF THE STRETCH REFLEX

1. ***Production of the skeletal muscle tone*** (see below).
2. ***Damping function*** : Through the ***alpha-gamma linkage*** (see below), signals discharged to the muscles are adjusted to produce smooth movements.
3. ***Increasing the power of muscle contraction (servo-assist function)*** : This also occurs through the alpha-gamma linkage, by the ***gamma-spindle loop mechanism*** (refer to text).

THE GAMMA EFFERENT SYSTEM

This is a system of efferent nerves that constitutes about 30 % of the efferent nerve fibres in the spinal ventral roots. They are type A gamma fibres that are the axons of small AHC called ***gamma motor neurons***. They supply the intrafusal muscle fibres in the muscle spindles and are ***2 types*** : *gamma-d fibres that supply the nuclear bag fibres and gamma-s fibres that supply the nuclear chain fibres*. Their discharge is controlled by several *supraspinal centres*(see later) and is increased in *anxiety*, by *noxious stimuli* and by *signals from contracting muscles* (see jendrassik maneuver below).

Alpha-gamma linkage (or coactivation)

Whenever the alpha motor neurons are activated (by signals from either the supraspinal centrers or the skeletal muscles), ***the gamma motor neurons are activated simultaneously***. This keeps the gamma motor neurons capable of adjusting the alpha motor neuron discharge reflexly throughout the movement, which is *important for both the damping as well as the servo-assist functions of the stretch reflex* (see above).

THE SKELETAL MUSCLE TONE

This is a state of *continuous subtetanic contraction of skeletal muscles during rest*. It is a ***static type of the stretch reflex*** that is produced as a result of mild continuous stretch of the muscles at rest. It is present in all muscles but specially in the ***antigravity muscles*** (because they are more stretched).

Functions of the muscle tone

1. It is essential for maintenance of the erect posture.
2. It helps the venous return and lymph flow specially from the lower limbs.
3. The tone of the anterior abdominal wall muscles prevents visceral ptosis.
4. It is an important source of heat production (so it increases in cold temp.).

THE TENDON JERKS

These are the responses of skeletal muscles to *sudden stretch* produced by tapping their tendons *strongly and sharply* (using a ***tendon hammer***). It is a ***dynamic type of the stretch reflex*** in which there is rapid contraction of the muscle followed by rapid relaxation. The common tested jerks are :

1. ***Knee (patellar) jerk***, the centre of which is the 2nd, 3rd and 4th lumbar segments. It can be reinforced by ***Jendrassik's maneuver*** (= grasping the hands together and pulling them apart strongly) which stimulates the gamma motor neurons(resulting in stretch of the muscle spindles and stronger contraction).
2. ***Ankle jerk***, the centre of which is the first and second sacral segments.
3. ***Biceps jerk***, the centre of which is the 5th and 6th cervical segments.
4. ***Triceps jerk***, the centre of which is the 6th and 7th cervical segments.
5. ***Radial and ulnar jerks***.
6. ***Jaw jerk***, which is a test for the integrity of the trigeminal (5th cranial) n.

Clinical importance of the tendon jerks

1. ***Localization of spinal cord lesions.***
2. ***Assessment of the muscle tone*** (exaggerated jerks usually occur with hypertonia, and vice versa).
3. ***Diagnosis of diseases*** (e.g. they are exaggerated in UMNL and lesion of area 6, weakened in neocerebellar lesions, chorea and lesion of area 4, and lost in LMNL and tabes dorsalis). In cases of hypotonia (specially in neocerebellar lesions and chorea), there is a ***pendular knee jerk***.

PROPERTIES OF THE STRETCH REFLEX

1- It is a *deep spinal reflex* the adequate stimulus of which is *muscle stretch*.
2- Its receptors are ***muscle spindles*** and its centre is ***alpha motor neurons***.
3- Its *reaction time is short* (19-24 ms) because it is ***monosynptic***, and its afferent and efferent neurons are ***rapidly conducting*** (A alpha fibres) .
4- It is ***highly localized***.
5- It shows almost ***no afterdischarge*** (because of absence of interneurons).
6- It shows ***reciprocal innervation, summation and rebound***.
7- It is subjected to control by *many supraspinal centres* (see below).
8- The *dynamic type is rapidly-adapting* while the *static type is slowly-adapting*.

9- The static type (skeletal muscle tone) is normally present in all muscles specially the ***antigravity muscles***.

10- The dynamic type is reinforced by ***Jendrassik's maneuver*** (see above).

11- The static type is inhibited by excessive stretch of the muscles through the ***inverse stretch reflex*** (see below).

12-The contraction is *smooth in the static type & jerky in the dynamic type*.

13-The static type is ***not-rapidly fatigued*** because **(a)** The spinal motor neurons discharge *at a low frequency and alternate their activity* **(b)** The O_2 *consumption during the reflex is not significantly increased*.

THE GOLGI TENDON ORGANS

These are ***tension receptors*** present in the tendons of skeletal muscles *in series with the muscle fibres*. They consist of netlike collections of knobby nerve endings that give rise to ***type Ib afferent nerve fibres***. They are stimulated by ***both passive stretch as well as active contraction of the muscles***.

Responses and effects of stimulation

As in case of the muscle spindles, the Golgi organs show ***dynamic and static responses***. However,opposite to these spindles, signals from the Golgi organs of a muscle *excite certain inhibitory neurons in the spinal cord* (*Golgi bottle neurons*) which ***inhibit the alpha and gamma motor neurons*** that supply this muscle, resulting in its relaxation. Accordingly, such ***negative induction reflex is disynaptic*** (in contrast, the MSR is monosynaptic).

Functions

1. They provide a *negative feedback mechanism that maintains the muscle tension constant and helps equalization of tension in different muscle fibres*.
2. Through the inverse stretch reflex (see next), they *prevent tearing of the muscles and avulsion of the tendons during strong muscle contractions*.

The inverse stretch reflex (autogenic inhibition)

This is *reflex relaxation of a muscle that occurs when the muscle tension increases markedly (e.g. due to excessive stretch of the muscle or a strong muscle contraction)*. It is a *protective inhibitory reflex* that is initiated as a result of *excitation of the Golgi tendon organs* (see above) and it acts during the lengthening reaction or clasp-knife effect (see next).

The lengthening reaction (= clasp-knife effect)

This reaction occurs in ***spastic muscles*** (e.g. in UMNL). It is elicited by passive flexion of a limb at its main joint (e.g. the lower limb at the knee joint). It consists of a *sequence of muscle contraction upon moderate stretch followed by sudden muscle relaxation upon over-stretch (the former by the stretch reflex and the latter by the inverse stretch reflex)*. Thus, during persistent flexion of the limb, there will be initial resistance that suddenly disappears and the limb flexes easily (as occurs ***during closing a pocket knife***).

Flexion of the limb is accompanied by extension of the contralateral limb. This *simulates the crossed extensor reflex*, and is called ***Philipson's reflex***.

The following table shows the differences between the stretch and inverse stretch reflexes :

	STRETCH REF.	INVERSE STRETCH REF.
Type	Monosynaptic	Disynaptic
Receptor	Muscle spindles	Golgi tendon organs
Stimulus	Muscle stretch (increased muscle length)	Excessive muscle stretch (increased muscle tension)
Effect	Muscle contraction	Muscle relaxation
Main functions	Maintenance of erect posture and smoothing movements	Prevents tearing of tendons during strong muscle contraction

Clonus : This is alternating rhythmic contractions and relaxations of a muscle in response to sudden maintained stretch. It can be elicited by forcible maintined pulling the patella downwards (***knee clonus***) or dorsiflexion of the foot (***ankle clonus***). It occurs *when the spinal motor neurons are excessively facilitated* (particularly in UMNL) and is due to ***a sequence of stretch reflexes and inverse stretch reflexes***.

HIGHER SUPRASPINAL CONTROL OF THE STRETCH REFLEX

(A) Supraspinal facilitatory areas

1. The facilitatory reticular formation (in the pons). *It is excited by all other facilitatory areas* and discharges via the *ventral reticulospinal tract* It produces its effects through stimulating ***the gamma motor neurons***.

2. The lateral vestibular nucleus(also stimulates the alpha motor neurons)

3. The neocerebellum. **4.** The primary cortical motor area 4 (also stimulates the alpha motor neurons).

5. The caudate nucleus of the basal ganglia. **6.** The inf.olivary nucleus.

(B) Supraspinal inhibitory areas

1. The inhibitory reticular formation (in the medulla). It is excited by all other inhibitory areas and discharges via the *lateral reticulospinal tract*. It produces its effects by inhibiting ***the gamma motor neurons***.
2. The red nucleus (also inhibits the alpha motor neurons).
3. The lentiform nucleus of the basal ganglia.
4. The paleocerebellum.
5. Certain cortical areas (areas 6 and 4 S).

Normally, ***the net effect of the cortical control is inhibition of the gamma motor activity***. This is because *the cortical inhibitory effect is much greater than the cortical facilitatory effect*. Accordingly, when both effects are simultaneously lost (e.g. in UMNL) the gamma motor activity increases, resulting in a type of hypertonia called ***gamma rigidity*** (see below).

DECEREBRATE RIGIDITY (DR)

This is a state of hypertonia that occurs in *decerebrate animals*, in which a transection is made *just above the pons or between the superior & inferior colliculi*. Such transection *abolishes the inhibitory effects of the red and lentiform nuclei as well as that of the cortical areas 6 and 4 S, but leaves the facilitatory reticular formation and the vestibular nuclei intact*. This increases the activity of both the alpha and gamma motor neurons, *specially the latter*, which results in ***gamma rigidity*** (see next).

GAMMA RIGIDITY AND ALPHA RIGIDITY

Gamma rigidity (= ***spasticity***) is muscle stiffness due to predominant overexcitation of the gamma motor neurons, while alpha rigidity is muscle stiffness due to predominant overexcitation of the alpha motor neurons. The following table summarizes ***the differences between both types of rigidity*** :

	GAMMA RIGIDITY	ALPHA RIGIDITY
Cause	Increased gamma activity	Increased alpha activity
Muscles affected	Antigravity muscles mainly	All muscles
Movement resistance	Uni-directional	Bi-directional
Type of rigidity	Clasp-knife	Lead-pipe or cog-wheel
Effect of velocity	Increases with velocity	Not velocity dependent
Tendon jerks	Exaggerated (with clonus also)	Not necessarily exaggerated
Common diseases	Upper motor neuron lesion	Parkinsonism

THE DESCENDING (MOTOR) TRACTS

These are divided into 2 main systems : ***pyramidal and extrapyramidal***.

(A) The pyramidal system

This consists of the ***corticospinal(= pyramidal) and corticobulbar tracts***, and possibly also the ***corticonuclear tract***. The latter tract arises from area 8 (see special senses) while the former 2 tracts arise from area 4 (30%), area 6 and supplementary motor area (30 %) and the somatic sensory areas (40 %), and ***90 % of their fibres cross to the opposite side through the lateral and ventral corticospinal tracts*** they exert the following functions :

(a) *Initiation of voluntary movements*, specially the discrete movements of the hands and fingers

(b) *Excitation of the cranial nerve nuclei and alpha spinal motor neurons*

(c) *Facilitation of the stretch and superficial reflexes.*

The respiratory and abdominal muscles also receive pyramidal fibres from the same side through ***the ipsilateral corticospinal tract***, so these muscles receive ***bilateral upper motor neuron (UMN) supply*** and accordingly, they are not paralyzed in cases of hemiplegia (page 39).

The medial and lateral motor systems

The ventral corticospinal tract and most extrapyramidal tracts (specially the vestibulospinal and reticulospinal tracts) form *a medial motor system which terminates at the medial portions of the anterior horns and controls the muscles of the trunk (the axial muscles).*

On the other hand, The lateral corticospinal tract and some extrapyramidal tracts (specially the rubrospinal tract) form *a lateral motor system which terminates at the lateral portions of the anterior horns and controls the distal muscles of the limbs that perform skill movements.*

(B) The extrapyramidal system

This system arises from widespread cortical areas (specially ***areas 6 & 4 S***) as well as from the ***basal ganglia***. The ***cortically-originating extrapyramidal fibres (C.O.E.P.)*** descend in the internal capsule ***mixed with the pyramidal fibres***, then some fibres pass directly to the brain stem while most fibres relay at the ***corpus striatum*** (part of the basal ganglia). The direct fibres and those originating from the basal ganglia transmit signals to the ***red nucleus, tectum of the midbrain, reticular formation, the vestibular and inferior olivary nuclei,*** from which the extrapyramidal tracts arise and descend to terminate *at the alpha or gamma spinal motor neurons*

PROPERTIES OF THE PYRAMIDAL (P) & EXTRAPYRAMIDAL (EXP) SYSTEMS

1. The origin of (P) is only cortical while that of (EX.P) is *both cortical and extracortical*.(from the basal ganglia).
2. The cortical origin of (EXP) is *much wider* than the origin of (P).
3. The pathway of (EXP) is *multineuronal* (indirect activation pathway) while that of (P) is *mononeuronal*(direct activation pathway)
4. The extrapyramidal tracts *do not occupy the medullary pyramids*.
5. About 90 % of pyramidal fibres cross to the opposite side, while only *about 50 % of extrapyramidal fibres cross*.
6. The (EXP) functions *during the first year of life* while (P) functions only after that age.
7. Some extrapyramidal tracts are facilitatory to the muscle tone and some are inhibitory (with predominance of the latter) while *the pyramidal tracts are only facilitatory*.
8. The extrapyramidal tracts terminate *only at the spinal motor neurons*, while the *pyramidal tracts terminate at both the alpha spinal motor neurons as well as the cranial nerve nuclei*.

FUNCTIONS OF THE EXTRAPYRMIDAL SYSTEM

1. Control of the axial muscles (= trunk muscles) and proximal muscles of the limbs, producing ***gross movements***.
2. Initiation of the subconscious (= associated or automatic) movements e.g. ***swinging of the arms during walking***.
3. Control of movements ***towards visual and auditory stimuli***, through the *tectospinal tracts* (see below).
4. An alternative route for performance of fine movements after injury of the pyramidal system, via the ***cortico-rubro-spinal pathway*** (see below).
5. Adjustment of the muscle tone and posture for maintenance of equilibrium and proper performance of fine skilled movements.
6. Control of autonomic functions through the *reticulospinal tracts* e.g. the ***visceral functions***.
7. The C.O.E.P. exert ***a powerful inhibitory effect*** on the gamma motor neurons and muscle tone.

THE EXTRAPYRMIDAL TRACTS

1- **Rubrospinal tract** : This tract arises from the *red nucleus* in the mid brain. It *crosses to the opposite side* then descends and terminates *at the alpha spinal motor neurons*. It receives fibres from the motor cortex, and the *cortico-rubro-spinal pathway serves as an accessory route for performance of fine movements* (see above). It *inhibits the alpha motor neurons and the muscle tone* and also mediates cerebellar signals to the spinal cord.

2- **Reticulospinal tracts** : The *lateral tract arises mainly in the medulla* and it crosses partially then descends. It is *inhibitory to the gamma motor neurons and muscle tone*. On the other hand, *the medial tract arises mainly in the pons* and it descends directly without crossing. It is *facilitatory* to *the gamma motor neurons and muscle tone*. Both tracts also control *autonomic functions by affecting the lateral horn cells*.

3- **Vestibulospinal tracts** : Both the lateral and ventral tracts arise from the vestibular nuclei in the medulla (specially the lateral vestibular nucleus). The ventral tract crosses partially then descends while the lateral tract descends directly and both terminate at *the alpha spinal motor neurons*. They are *facilitatory to the muscle tone* and also mediate some postural reflexes.

4- **Tectospinal tracts** : Both the lateral and ventral tracts arise from the *tectum of the midbrain* then cross and descend to terminate at the motor neurons of the *cervical segments of the spinal cord*. The ***lateral tract arises at the superior colliculi and mediates visuospinal reflexes*** while the ***ventral tract arises at the inferior colliculi and mediates auditoryspinal reflexes***.

5- **Olivospinal tract** : This tract originates at the *inferior olivary nucleus* in the medulla. It *crosses to the opposite side* then descends and terminates *at the motor neurons of the cervical segments of the spinal cord*. It is *facilitatory to the muscle tone* and is also a possible route for transmission of signals from the cerebellum and basal ganglia to the spinal cord.

SOME COMMON LESIONS IN THE CNS

(1) UPPER AND LOWER MOTOR NEURON LESIONS

Upper motor neuron lesions (*UMNL*) result from damage of the cortical motor areas or injuries anywhere along the course of their descending tracts commonly in ***the internal capsule***. On the other hand, lower motor neuron lesions (*LMNL*) result from damage of the spinal (or cranial) motor neurons (e.g. due to *poliomyelitis*), or injuries of their motor nerves.

Both UMNL and LMNL cause ***paralysis of skeletal muscles***. However each produces characteristic manifestations, as shown in the following table

	UMNL	LMNL
Extent of paralysis	Widespread	Localized
Site of paralysis	Contralateral or ipsilateral	Always ipsilateral
Recovery	Never occurs due to absence of neurolemma	Can occur (if the motor neurons are intact)
Muscle tone	Hypertonia (gamma rigidity)	Hypotonia or atonia
Tendon jerks	Exaggerated (with clonus)	Lost
Superficial reflexes	Lost with +ve Babinski's sign	Lost
Tonic neck reflexes	Present	Absent
Muscle status	Normal (late disuse atrophy)	Rapid atrophy
Response to electric stim.	Normal	Reaction of degeneration

BABINSKI'S SIGN

Scratching the lateral edge of the sole (e.g. by a key) causes ***dorsiflexion of the big toe and fanning of the other toes***. Such response is a part of the flexor withdrawal reflex and is ***normally absent (because it is inhibited by the pyramidal tracts)*** and the *normal plantar reflex (plantar flexion of all toes) occurs instead*. Accordingly, it appears (i.e. becomes +ve) when these tracts are *interrupted* (e.g. in UMNL) or *not functioning* (e.g. in normal infants below1 year of age and normal adults during sleep,coma or anaesthesia).

THE REACTION OF DEGENERATION (RD)

This is an abnormal response to electric stimulation that ***occurs only in LMNL***, and is characterized by the following :

1. There is no response to Faradic currents.
2. There is a sluggish (i.e. weak) response to Galvanic currents.
3. The anodal closing contraction (ACC) becomes stronger than the cathodal closing contraction (CCC) by unknown causes (the opposite is the normal).
4. The chronaxie of the paralyzed muscles is prolonged.

(2) LESIONS OF THE PYRAMIDAL TRACTS AT VARIOUS LEVELS

These lesions cause paralysis of the ***UMNL type below the level of the lesion***, the extent of which depend on the site of lesion as shown in the following table :

SITE OF LESION	EFFECTS OF LESION
Area 4	Almost always *contralateral monoplegia*
Corona radiata	*Contralateral monoplegia or hemiplegia* (depending on the extent of lesion)
Internal capsule	Almost always *contralateral hemiplegia*
Brain stem	*Contralateral hemiplegia + Ipsilateral LMNL* paralysis of *some cranial nerves* due to damage of their nuclei (the affected cranial nerves depend on the site of lesion)
Spinal cord	-Unilateral cervical lesions cause *ipsilateral hemiplegia* while unilateral midthoracic lesions cause *ipsilateral monoplegia in the corresponding lower limb*. -Bilateral cervical lesions cause *quadriplegia* (paralysis of the 4 limbs). while bilateral midthoracic lesions cause *paraplegia* (paralysis of the 2 lower limbs)

(3) COMPLETE TRANSECTION OF THE SPINAL CORD

Patients with this lesion pass in 3 stages (1) Spinal shock (2) Recovery of spinal reflex activity (3) Failure of such activity and death.

MANIFESTATIONS OF SPINAL SHOCK

1. Loss of all sensations below the level of the lesion.
2. Quadriplegia or paraplegia (according to the site of the lesion).
3. V.D. below the level of the lesion (which may lead to *hypotension*).
4. Bilateral miosis (in cases of cervical lesions only).
5. Absence of spinal reflex activity below the level of the lesion due to

sudden withdrawal of supraspinal facilitation on the spinal alpha motor neurons, resulting in the following manifestations :

a- Loss of the withdrawal reflex (which may lead to *skin injuries*).

b- *Muscle flaccidity* (due to loss of the stretch reflex).

c- Loss of the erection, defecation and micturition reflexes (resulting in *urine retention with overflow*).

Duration and management of spinal shock

In humans, such manifestations last for a long time ***(2-6 weeks)*** *due to the high degree of encephalization in man*. However, the case can be ***managed to enhance recovery*** by **(a)** Giving spinal stimulants and antibiotics (to prevent infections) **(b)** Adequate nutrition **(c)** Cleaning the skin and frequent changing the patient' position in bed (to prevent bed sores) **(d)** Frequent bladder catheterization (to prevent infection of the urinary tract).

STAGE OF RECOVERY OF SPINAL REFLEX ACTIVITY

This occurs gradually as follows :

1. The flexor reflexes recover first (so a +ve Babinski's sign appears) followed by the extensor reflexes (e.g. the knee jerk).
2. The static stretch reflex (muscle tone) recovers resulting in ***spastic paralysis***, first in the flexor muscles then in the extensor muscles.
3. The spinal vasomotor centres (lateral horn cells) recover and discharge, leading to V.C. (so the arterial B.P. rises towards the normal level).
4. Reflex micturition and defecation is restored but they are ***automatic*** (due to absence of the voluntary control).
5. Appearance of the **mass reflex** after a few months : Stimulation of the skin *below the level of lesion by mild noxious stimuli* results in **(a)** Powerful withdrawal of the limb **(b)** Urination and defecation **(c)** V.C. and profuse sweating **(d)** Fluctuation (usually rise) of the arterial blood pressure

STAGE OF FAILURE OF SPINAL REFLEX ACTIVITY

This is a ***terminal stage*** that occurs due to bad management of the case. It is associated with ***toxaemia*** secondary to bed sore or urinary infection. The spinal centres below the level of the lesion are depressed leading to **(a)** Loss of the muscle tone, so the *muscles become flaccid* **(b)** Loss of the mass and withdrawal reflexes and disappearance of Babinski's sign **(c)** Loss of the defecation and micturition reflexes (*resulting in urine retention with overflow*) **(d)** Depression of the spinal V.C. centres, resulting in *hypotension*.

(4) HEMISECTION OF THE SPINAL CORD (Brown-Sequard syndrome)

This lesion causes the following manifestations :

(A) Above the level of the lesion : Cutaneous hyperesthesia occurs in the *ipsilateral dermatomes* innervated by the dorsal roots that enter the spinal cord just above the level of the lesion (due to irritation of these roots).

(B) At the level of the lesion : The following occurs ***in the same side*** :

1. Loss of all sensations in the areas innervated by the afferent nerves that enter the damaged spinal segments.
2. LMNL paralysis of the muscles supplied by the efferent nerves that arise from the damaged spinal segments (due to damage of the AHC)..
3. Loss of all reflexes mediated via the damaged spinal segments.

(C) Below the level of the lesion :

1. The following occurs ***in the same side*** **(a)** UMNL paralysis due to interruption of the ipsilateral pyramidal tract **(b)** V.D. due to interruption of the ipsilateral vasomotor tract **(c)** Miosis (in case of cervical lesions) or horner's syndrome if the ipsilateral sympathetic fibres are damaged **(d)** Loss of all sensations mediated by the ipsilateral gracile and cuneate tracts (page 10)
2. ***Loss of pain and temperature sensations in the opposite side*** due to interruption of the contralateral lateral spinothalamic tract.
3. ***Weakening (not loss) of crude touch sensation in both sides*** (because it is transmitted by both the ventral spinothalamic and dorsal column tracts.

(5) QUADRANT LESIONS OF THE SPINAL CORD

(1) Anterior quadrant lesion : This leads to the following :

(a) Contralateral loss of pain and temperature sensations *below the level of the lesion* (due to interruption of the contralateral lateral spinothalamic tract.

(b) Ipsilateral LMNL paralysis of the muscles and loss of the reflexes *at the level of the lesion* (due to damage of the spinal motor neurons).

(2) Posterior quadrant lesion : This leads to the following ***at the same side of the lesion*** :

(a) UMNL paralysis and loss of all sensations transmitted by the dorsal column tracts ***below the level of the lesion***.

(b) Loss of all sensations and reflexes from the areas innervated by the dorsal nerve roots that enter the spinal cord ***at the level of the lesion*** (due to damage of these roots).

(6) LESION OF THE POSTERIOR LIMB OF THE INTERNAL CAPSULE

The internal capsule (= ***porta cerebri***) is the *only pathway to and from the cerebral cortex*. Lesions of its posterior limb are commonly due to *thrombosis or haemorrhage of the lenticulo-striate artery*. Such lesions are usually unilateral, and the patient passes in ***2 stages*** :

(A) Acute stage (a few days up to 2- 3 weeks)

This is a stage of ***acute UMNL*** that shows manifestations similar to those of spinal shock ***in the opposite side***. They include the following :

1. Flaccid paralysis.
2. Hemianaesthesia (i.e. complete loss of all sensations).
3. Hypotonia (or atonia) and hyporeflexia (or areflexia).
4. Loss of superficial reflexes and may be +ve Babinski's sign.

(B) Chronic stage

This stage shows the following manifestations :

1. **Contralateral hemiplegia of the UMNL type** (characterized by hypertonia, muscle spasticity of the clasp-knife type, exaggerated tendon jerks with clonus, loss of superficial reflexes, and apparent +ve Babinski's sign and tonic neck reflexes). The respiratory and abdominal muscles are not affected because they receive *a bilateral UMN supply* (page 32). Partial recovery occurs after a variable period of time by the effect of the *ipsilateral corticospinal tract* (page 32)as well as the *cortico-rubro-spinal pathway* (page 34).
2. **Permanent contrtalateral loss of fine (cortical or epicritic) sensations** but the crude (thalamic or protopathic) sensations recover gradually.
3. **Contralateral (crossed) homonymous hemianopia**. This is loss of vision in the opposite halves of the 2 visual fields. It is due to damage of the optic radiation, which interrupts signals from the temporal half of the ipsilateral retina and the nasal half of the contralateral retina (refer to the visual nervous pathway in special senses).
4. **Diminished power of hearing in both ears by about 50 %** : This is due to damage of the auditory radiation which interrupts signals from the cochleae of *both ears* (refer to the auditory nervous pathway in special senses).

CHAPTER 7

THE THALAMUS

This is a subcortical mass of grey matter that contains the following nuclei

:(A) **Nonspecific projection nuclei** : These include mainly ***the middle and intra laminar nuclei***. They receive signals from the *reticular formation* and discharge to almost all areas of the cerebral cortex.

(B) **Specific projection nuclei** :

1. **Ventro-posterior nucleus** : Its lateral part *(VPLN)* receives the spinal lemniscus while its medial part *(VPMN)* receives the trigeminal lemniscus, then both parts project to the sensory cortical areas in the postcentral gyrus.
2. **Lateral geniculate nucleus (or body)** : This projects visual signals to the visual cortical areas in the occipital lobe.
3. **Medial geniculate nucleus (or body)** : This projects auditory signals to the uditory cortical areas in the temporal lobe.
4. **Ventro-lateral nucleus** : This is the *main thalamic motor nucleus* that receives signals from the cerebellum and basal ganglia and projects to the cortical motor areas.
5. **Anterior nucleus** : This receives signals from the *hypothalamus* and discharges to the *limbic lobe*.
6. **Dorsal nuclei (medial and lateral)** : These are association nuclei that receive signals from other thalamic nuclei then project to the prefrontal cortical area (medial nucleus) and the cortical association areas (lateral nucleus).

FUNCTIONS OF THE THALAMUS

1. It conveys all sensations to the cerebral cortex ***except smell*** (it is a relay station in the pathway of ***epicritic sensations from the opposite side*** as well as in the pathways of ***vision and hearing***).

2. The nonspecific nuclei are relay station in the *ARAS*(Ascending Reticular Activating System) and are probably the centre of ***protopathic sensations***.

3. It is a relay station for signals to the cortical motor areas from the *contralateral cerebellum & ipsilateral basal ganglia* (that coordinate movements).

4. It shares in the control of the ***high intellectual functions of the cerebral cortex and the emotional reactions***.
5. It is a part of the system that determines the ***behaviour and personlity*** of the individual.
6. It is one of the areas concerned with preservation of ***memory*** (page 59).

THE THALAMIC SYNDROME

This is a disease that occurs as a result of ***thrombosis of the thalamo-geniculte artery***, and it leads to the following manifestations in the ***opposite side of the body :***

1. Early in the disease, there is *complete loss of all sensations* (however, the ***facial sensations are usually retained*** because the damage occurs mainly in the VPLN while the VPMN is little affected).

2. Loss of the kinesthetic sensations results in ***sensory ataxia***, as in tabes dorsalis (page 12).

3. Within a few weeks or months, the crude (protopathic) sensations recover gradually and are associated with *emotional disturbances and hyperpathia*.

4. The fine (epicritic) sensations are permanently lost together with loss of tactile localization and discrimination as well as ***astereognosis***.

5. Hypotonia, asthenia and ***motor ataxia*** as a result of *loss of the cerebellar control on the cortical motor areas* (therefore in this disease, the ***ataxia is mixed*** i.e. both sensory and motor, page 51).

6. Involuntary movements (as those produced in chorea and athetosis) occur as a result of *interruption of the circuits that connect the basal ganglia to the cerebral cortex* (page 46).

CHAPTER 8

THE HYPOTHALAMUS

This is a part of the *diencephalon* that contains the following nuclei :

1. Anterior group (specially the *supraoptic nd paraventricular nuclei*).
2. Lateral group (a large lateral nucleus).
3. Medial group (the dorsomedial and ventromedial nuclei).
4. Posterior group (specially the mamillary nuclei in the *mamillary body*).
5. Periventricular nuclei (part of the *analgesia system*, page 14).

FUNCTIONS OF THE HYPOTHALAMUS

1. **Control of autonomic functions** : Parasymp.functions are controlled by the anterior nuclei, and symp.functions by the lateral & posterior nuclei.

2. **Control of endocrine glands** :The hypothalamus controls the ***posterior pituitary gland & the adrenal medulla*** directly ***(i.e. by nervous control)*** while it controls ***most of the other endocrine glands*** indirectly ***by regulating the activity of the anterior pituitary gland*** through secreting the hypothalamic hormones called *hypophysiotropic hormones* (refer to endocrines). Through the endocrine control, the *hypothalmus regulates the metabolism*.

3. **Regulation of body temperature** : This occurs through the hypothalamic ***thermoreceptors*** as well as the ***thermoregultory centre*** which consists of a *heat loss centre* in the anterior nuclei and *a heat gain centre* in the posterior nuclei (refer to energy metabolism).

4. **Control of water balance** : This occurs through the hypothalamic ***osmoreceptors*** that regulate both ***water gain*** (by acting as ***a thirst centre***) as well as ***water loss*** by controlling release of the antidiuretic hormone ***(ADH)*** from the posterior pituitary gland (refer to kidney).

5. **Control of food intake** : This occurs through the ***hypothalamic appestat centre*** which consists of ***a feeding centre in the lateral nuclei*** and a ***satiety centre in the ventromedial nucleus***. There is also a ***salt appetite centre*** in the anterior hypothalamic nuclei that regulates the salt intake.

6. **Control of circadian rhythms :** There are dominant pacemakers in the hypothalamus (specially in the ***suprachiasmatic nuclei***) that control many circadian rhythms in the body e.g. *the rhythmic secretion of ACTH and melatonin, the sleep-wake cycles and the body temperature rhythm*.

7. **Regulation of sexual functions :** This occurs by regulating the release of the ***gonadotropic hormones*** from the anterior pituitary gland. The anterior hypothalamic nuclei are also excited by the circulating estrogens and androgens resulting in increased libido.

8. **Control of motivation, learning and memory :** This is produced *together with other areas, specially the limbic system* (page 59).

9. **Relation to sleep :** The hypothalamus has no direct role in the regulation of sleep because it *contains no sleep or wakefulness centres*. The somnolence (= hypersomnia) that occurs in some hypothalamic disorders is due to interruption of ascending subhypothalamic pathways that control sleep.

10. **Control of emotional expression (reactions) :** The expression of emotions involves activity of the hypothalmus, limbic system and the prefrontal lobe. The commonest emotions are ***rage and fear***, and the reaction to either includes *autonomic responses* (mostly sympathetic) and *somatic responses* e.g. turning the head from side to side in case of fear (seeking escape) and biting and clawing in case of rage.

There is a ***fear centre*** in the periventricular nucleus of the hypothalamus and ***a rage centre*** in its lateral nuclei. There is also ***a placidity centre*** in the ventromedial nucleus, and the emotional state of the subject is determined by the *balance between the activity of this centre and the rage centre*

The sham rage reaction

The rage centre is normally inhibited by the placidity centre and the neocortex, and stimulted by the amygdaloid nucleus. The sham rage reaction is a ***violent reaction in response to minor stimuli***. It occurs as a result of either *lesions of the neocortex or the placidity centre or excitation of the amygdaloid nucleus*, and it includes **(a)** Sympathetic responses e.g. tachycardia, piloerection and mydriasis **(b)** Somatic responses e.g. biting and clawing, hissing, spitting and growling (specially in cats).

Effects of hypothalamic lesions

1. *Endocrinal disturbances* e.g. diabetes insipidus and Frohlich's syndrome.
2. *Disturbances of the body temperature* (hyperthermia or hypothermia).
3. *Sleep disturbances* (e.g. hypersomnia, narcolepsy or insomnia).
4. Abnormal appetite (hyperphagia or anorexia).
5. *Disturbances in motivation, memory and learning*.
6. *Autonomic disturbances* (e.g. spontaneous V.C. or V.D. and sweating).
7. Abnormal emotions (e.g. fear, rage or placidity).
8. Sexual disturbances.

FUNCTIONS OF THE LIMBIC SYSTEM

The limbic system consists of the *limbic lobe of the cerebral cortex and certain subcortical structures (e.g. the hypothalamus, the amygdaloid nuclei, the hippocampus, the fornix and the anterior thalamic nucleus)*. This system performs the following functions :

1. Perception of the ***olfactory (smell) sensation***.
2. It shares in the control of ***autonomic functions*** (mostly as a part of the emotional responses).
3. Control of ***sexual behaviour*** (specially by the amygdaloid nuclei).
4. It is greatly involved in the development of ***memory*** (specially the hippocampus, page 59)
5. ***Control of emotions*** (together with the hypothalamus), specially by the amygdaloid nuclei.
6. ***Control of motivation*** : This is a function of the following systems :

a- The reward (or approach) system : This includes the *reward centre in the hypothalamus* as well as less potent centres in the amygdaloid nuclei, the thalamus and the basal ganglia. Its stimulation produces a sense of pleasure and increases motivation.

b- The punishment (or avoidance) system : This includes the *punishment centre in the hypothalamus* as well as less potent centres in the amygdaloid nuclei and the hippocampus. Its stimulation produces a sense of displeasure, fear or terror, and decreases motivation.

THE BASAL GANGLIA

These are subcortical masses of gray matter that include the following :

1. *The caudate nucleus.*
2. *The lentiform (or lenticular) nucleus* : This consists of the *putamen and globus pallidus*. The ***caudate nucleus + putamen = corpus striatum***
3. *The subthalamic nucleus.*
4. *The substantia nigra (in the midbrain).*

CONNECTIONS OF THE BASAL GANGLIA

These are divided into **3 parts** :

(A) Cortical connections : These include *2 feedback circuits* :

*1. **Putamen circuit*** [Cortical somatic sensory areas and motor association areas (premotor and supplemental motor areas) → putamen → globus pallidus → thalamic ventrolateral nucleus (directly and through the subthalamic nucleus and substantia nigra)→ Cortical motor area 4].

*2. **Caudate circuit*** [Cortical sensory and motor association areas → caudate nucleus → globus pallidus → thalamic ventrolateral nucleus→ Cortical motor association areas].

(B) Inter- connections : These include 2 main connections :

1. A dopaminergic nigro-striatal connection.

2. A GABA striato-nigral and striato-pallidal connections.

Other transmitters in the basal ganglia include *acetylcholine* (from the cortical neurons) as well as *norepinephrine, serotonin and enkephalin* (from brain stem projections).

(C) Brain stem connections : These are connections to the ***reticular formation as well as to the red, vestibular and inferior olivary nuclei.***

FUNCTIONS OF THE BASAL GANGLIA

These functions are **only motor**, and include the following :

(1) Control of muscle tone : The ***lentiform nucleus decreases the muscle tone*** by inhibiting the cortical motor areas and the vestibular nucleus (which decreases the activity of the *alpha spinal motor neurons*). On the other hand, the ***caudate nucleus increases the muscle tone*** by exciting the facilitatory reticular formation, the vestibular nucleus and the inferior olivary nucleus.

(2) Control of voluntary movements : The basal ganglia (with the cortical motor areas and the cerebellum) are required for performance of skilled voluntary movements. They discharge ***before the movements start*** and are concerned with ***planning and programming of motor actions***. The *putamen circuit stores the programs of learned patterns of motor activity, while the caudate circuit converts new thoughts into fine motor actions* .

(3) Initiation of associated (automatic) movements : The basal ganglia share the extrapyramidal cortical areas in initiating such movements *subconsciously* e.g. swinging of the arms during walking (page 33). The basal ganglia also produce *postural adjustments that maintain equilibrium during the voluntary movements*.

DISEASES OF THE BASAL GANGLIA

(1) CHOREA :This disease may be hereditary (*Huntington's chorea*) or acquired, often after rheumatic fever (*Sydenham's chorea*). It is due to *damage of the corpus striatum specially the caudate nucleus*, which is associated with ***degeneration of the GABA neurons***. It is characterized by :

a- *Rapid purposeless involuntary dancing movements that occur suddenly in the opposite side during rest*. They are due to *increased activity of the cortical motor areas* caused by *excessive discharge of excitatory signals to these areas from the globus pallidus and substantia nigra* (due to their release from inhibition as a result of GABA deficiency).

b- *Hypotonia and pendular knee jerk*, due to loss of the facilitatory effect of the caudate nucleus on the stretch reflex (page 28).

c- *Dementia* (decrease of the intellectual functions specially memory) due to simultaneous degenertion of the cholinergic neurons in the cerebral cortex.

(2) ATHETOSIS : This is due to damage of the *lentiform nucleus specially the globus pallidus*. Loss of the inhibitory effect of the lentiform nucleus leads to ***contralateral** hypertonia and involuntary spasmodic slow writhing movements* specially in the face and hands, resulting in *abnormal postures that are not kept at a fixed position*.

(3) HEMIBALLISMUS : This is due to damage of the *subthalamic nucleus*. Loss of the inhibitory effect of the putamen circuit leads to over-excitation of the cortical motor areas, resulting in contralateral *hypertonia as well as* *violent rapid spasmodic involuntary movements.*

(4) **PARKINSONISM (PARALYSIS AGITANS)**: This is due to damage of the *substantia nigra* which leads to ***marked reduction of the dopamine content in the basal ganglia***. It often occurs as a complication of *atherosclerosis or prolonged use of the phenothiazine tranquilizers*. It is characterized by :

a- **Muscle rigidity** : This specially occurs in the *flexor muscles*. Its pattern is either *lead-pipe or cog-wheel* and is associated with *normal tendon jerks*. It is an *alpha rigidity* that occurs due to *release of the corpus striatum from the inhibitory effect of dopamine (so the corpus striatum discharges excessive excitatory signals to the cortical motor areas and the vestibular nuclei*, which in turn discharge excessively to the spinal alpha motor neurons resulting in their overexcitation (which leads to alpha rigidity).

b- **Akinesia or hypokinesia** : This is manifested by *difficulty in initiating voluntary movements, mask face, slow monotonous speech, shuffling gait and absence of the associated movements*. It is also due to loss of the inhibitory effect of dopamine, which *locks the basal ganglia at a state of excitation and renders them unable to planning and programming of movements* resulting in difficulty in initiating movements & their sequential progression

c- **Static tremors** : These occur *during rest* and disappear during sleep and on performance of voluntary movements. They are fine involuntary rhythmic movements produced by *alternating contractions of antagonistic muscles*. They are most marked in the *hands and fingers* (where they often appear as *pill rolling movements*). They are probably due to *oscillation of activity in the feedback circuits after loss of their inhibitory effect*.

Treatment of Parkinsonism

1- *Increasing the dopamine content in the basal ganglia*, by giving ***L-dopa*** (which *can cross the blood brain barrier*) or ***L-deprenyl*** (*which blocks the monoamine oxidase enzyme that inactivates dopamine*).

2- *Decreasing the excitatory effect of acetylcholine in the basal ganglia*, by giving ***anticholinergic drugs*** (e.g. atropine).

3- *Blocking the excitatory signals discharged from the corpus striatum* to the cortical motor areas, by ***destructing the ventrolateral thalamic nucleus*** (using electrocoagulation).

CHAPTER 10

THE CEREBELLUM

From the functional point of view, the cerebellum is divided into **3 parts** :

1- ***Archicerebellum (vestibulocerebellum)*** : This consists of the flocculonodular lobe and adjacent portions of the vermis.

2- ***Spinocerebellum (paleocerebellum)*** : This consists of the intermediate zones of the 2 cerebellar hemispheres and most of the vermis.

3- ***Cerebrocerebellum (neocerebellum)*** : This consists of the large lateral zones of the 2 cerebellar hemispheres.

STRUCTURE AND CONNECTIONS OF THE CEREBELUM (CB)

The CB is formed of an ***outer cortex*** (gray matter) and ***inner white matter that contains 3 deep nuclei*** called the ***dentate, fastigial and interpositus nuclei***. The afferent and efferent fibres of the CB pass via ***3 peduncles*** called the ***superior ,middle and inferior cerebellar peduncles***.

The CB receives **afferent fibres** from the following :

1. The spinocerebellar tracts.
2. The reticular formation.
3. The inferior olivary nucleus.
4. The tectum (of the midbrain).
5. The vestibular apparatus (both directly and via the vestibular nuclei).
6. The contralateral cortical motor areas (*cortico-ponto-cerebellar pathway*).
7. The gracile and cuneate nuclei.

The afferent fibres are divided into 2 groups called **climbing fibres** (those from the inferior olivary nucleus) and **mossy fibres** (all other afferent fibres). Both groups give first *excitatory collaterals to the deep nuclear cells* (**DNC**) then proceed upwards and excite the Purkinje cells (**PC**) in the cerebellar cortex (directly by the climbing fibres, and via the *granule cells* in case of the mossy fibres). The axons of the PC are the *only fibres that leave the cerebellar cortex and their only action is inhibition of the DNC*.

As a result of this arrangement, when afferent signals reach the CB, the DNC first receive excitatory ***"turn on"*** signals that stimulate them to discharge, then within a few milliseconds, they receive inhibitory ***"turn off"*** signals from the PC that stop their discharge.

In case of the mossy fibres, this helps precise execution of voluntary movements, because the turn on signals help initiation of the movement while the turn off signals help its termination without overshooting. On the other hand, *in case of the climbing fibres, these signals are important for learning the CB to perform new patterns of movement precisely.*

The **efferent fibres** from the CB are *axons of the DNC* and they reach

1. The vestibular nuclei.
2. The reticular formation.
3. The red nucleus.
4. The *contralateral thalamus*; in which the efferent fibres relay mostly in the *ventrolateral nucleus* From the latter, signals are then discharged to the contralateral basal ganglia as well as the *contralateral cortical motor areas* (= *cerebello-dentato-thalamo-cortical pathway*).

FUNCTIONS OF THE CEREBELUM (CB)

The CB is concerned with ***subconscious control of motor activity*** through the following functions :

1- **Control of equilibrium** : This is the function of the *vestibulocerebellum* through afferent and efferent connections with the vestibular apparatus.

2- **Control of the stretch reflex** : The cerebrocerebellum exerts a facilitatory effect on the stretch reflex, while the spinocerebellum exerts an inhibitory effect. However, the facilitatory effect is predominant in man.

The cerebellar stretch reflex

Signals from the muscle spindles are transmitted to the CB (via the spinocerebellar tracts), which responds by discharging signals downwards (via the reticulospinal tracts) that excite the spinal motor neurons, resulting in muscle contraction. This reflex is ***more complex than the spinal cord reflex and its feedback time is much longer***. It produces ***postural adjustments*** and is also concerned with the ***damping function of the CB*** (see below).

3- **Control of voluntary movements** :

(A) **Role of the spinocerebellum** :

1. Servocomparator function : The spinocerebellum receives an ***afference copy*** of the signals discharged from the motor cortex for performance of a certain movement (via the *cortico-ponto-cerebellar pathway*), and an ***efference copy*** of signals from the contracting muscles (via the ***spinocerebellar tracts***). It ***compares both informations***, then sends signals to both the

motor cortex and the red nucleus which in turn send correcting signals to the spinal motor neurons that adjust the performance to match the intended movement (which leads to a coordinated and purposeful movement).

2. Damping function :The spinocerebellum acts ***as a brake*** that stops the movement at the intended point (thus preventing overshooting and pendular movements). Such effect is produced by contraction of the antagonistic muscles through the *cerebellar stretch reflex* (see above).

3. Coordination of ballistic (very rapid) movements : This occurs by potentiating their start and helping their termination through ***the turn on / turn off*** signals produced by the *mossy fibres* (page 48).

(B) Role of the cerebrocerebellum :

1. Planning of movements : The cerebrocerebellum receives signals from the cortical motor association areas and discharges before the movement starts (like the basal ganglia),and both provide the plan of the sequential movements required to execute the intended voluntary movement.

2. Prediction of movements :The cerebrocerebellum has the ability to display the plan of the next sequential movement at the same time the present movement is occurring. This helps joining of the sequential movements, which smoothes the voluntary movement and prevents its decomposition.

3. Timing of movements : The cerebrocerebellum predicts how far a movement will go in a given time, then provides appropriate timing for each sequential movement. So in its absence, such movements may start early or late than they have to (resulting in incoordination of voluntary movements and failure of their smooth progression, specially if rapid or complex).

THE NEOCEREBELLAR SYNDROME

This is a disease caused by damage of the CB (*specially the deep nuclei*). Its manifestations appear at the ***ipsilateral side***, and include the following :

(A) Hypotonia associated with pendular knee jerk (page 28).

(B) Asthenia (muscle weakness) due to difficulty in initiating and potentiating the movements (caused by loss of the functions of the mossy fibres).

(C) Motor (cerebellar) ataxia : This is incoordination of voluntary movements, the signs of which include the following :

1. *Dysmetria* (inability to control the distance of a motor act).
2. *Kinetic tremors* (= intention or terminal tremors).
3. *Rebound* (overshooting of a limb due to loss of the braking function).
4. *Asynergia* (loss of harmony between the various muscle groups).

5. *Failure of progression of movements* : This is manifested by :
    - *Adiadokokinesia* (inability to perform rapid alternate movements).
    - *Decomposition (fragmentation) of movements.*
6. *Dysarthria* (staccato or scanning speech).
7. *Nystagmus* (tremor of the eyeball on fixing the eye at an object).
8. *Staggering (drunken) gait.*

TYPES AND CAUSES OF TREMORS

1. *Static tremors* (occur in Parkinsonism).
2. *Kinetic tremors* (occur in the neocerebellar syndrome).
3. *Fine tremors* (occur in hyperthyroidism).
4. *Flapping tremors* (occur in liver failure).
5. *Senile tremors* (occur in old age).
6. *Emotional and psychological tremors.*
7. *Familial and hereditary tremors.*
8. *Toxic tremors* (caused by certain toxins e.g. in chronic alcohol drinkers).

TYPES OF ATAXIA

Ataxia is either ***sensory, motor or mixed*** e.g. in the thalamic syndrome (page 41). The following table summarizes the differences between motor and sensory ataxia :

	SENSORY ATAXIA	MOTOR ATAXIA
Commonest cause	Tabes dorsalis	Neocerebellar syndrome
Gait	Stamping (high steppage)	Staggering (drunken)
Romberg's sign	Positive	negative
Effect of vision	Can correct the ataxia	No effect
Dorsal column sensations	Impaired or lost	Normal
Tremors	Absent	Kinetic (intention) tremors
Nystagmus	Absent	Present
Speech	Normal	Scanning or staccato

CHAPTER 11

THE CEREBRAL CORTEX

The cerebral cortex contains the *highest centres in the CNS*, and is concerned with perception of the *fine (epicritic) sensations and initiation of skilled voluntary movements, as well as consciousness and the high intellectual functions (e.g. speech, learning, memory, planning, judgement, etc.).* it is divided into *2 large hemispheres*, each of which contains *5 lobes (frontal, temporal, parietal, occipital and limbic lobes)*. The latter is a part of the limbic system and its functions were discussed before (page 44) while the areas present in the other lobes and their functions are as follows

THE FRONTAL LOBE

This lobe contains the cortical motor areas 4, 6, and 8, the suppressor strip (= area 4 S, page 31), and the supplementary (or supplemental) motor area as well as the prefrontal association area (areas 9, 10 and 11).

The primary motor cortex or area (area 4)

This area is located in the ***precentral gyrus***. It controls muscle activity mainly ***in the opposite side of the body***,and in it the body is represented in an ***inverted manner***. It contains the large ***Betz cells***, and is the origin of about 30% of the pyramidal tract fibres. It performs the following functions:

1. It initiates fine discrete voluntary movements specially in hands & fingers

2. It shares area 6 in initiating gross movements.

3. It exerts a facilitatory effect on the stretch reflex.

4. It is necessary for occurrence of the superficial reflexes.

Lesions of area 4 lead to the following in the *opposite side of the body*:

1. Paralysis of skeletal muscles, commonly monoplegia (page 36) with permanent loss of skilled movements (but gross movemenys are only lost temporarily).

2. Inhibition of the stretch reflex (so the paralyzed muscles are flaccid and the tendon jerks are weak).

3. Loss of the superficial reflexes.

4. +ve Babinski's sign (mainly ***dorsiflexion of the big toe***).

The premotor cortex

This contains area 6, area 4 S and the supplementary (or supplemental) motor area, as well as areas 44 (Broca's area) and area 8 (see below).

Functions of area 6 (premotor area or motor association area)

1. It shares in *planning of voluntary movements*.
2. It initiates *gross movements* (with area 4).
3. It *inhibits the stretch reflex and muscle tone* (with area 4 S).
4. It shares in controlling *autonomic functions*.(with the limbic system).
5. It *inhibits the grasp reflex* (page 66).
6. It initiates the *subconscious associated movements* with the basal ganglia.
7. It is necessary for the *normal response of the plantar reflex*.
8. It contains areas that perform highly specialized functions : **(a)** Broca's area that is essential for *normal speech* **(b)** Eye movement area (area 8) **(c)** Head rotation area **(d)** Hand skills area.

Therefore, **lesions of area 6** produces the following symptoms in the opposite side :

1. *Muscle paresis* (weakness) and temporary absence of gross movements.
2. *Muscle spasticity* (increased muscle tone) and exaggerated tendon jerks
3. +ve Babinski's sign (mainly ***fanning of the toes***).
4. *Appearance of the grasp reflex* (page 66).
5. *Autonomic disturbances*.
6. *Loss of voluntary eye movements and head rotation*.
7. ***Motor aphasia*** due to damage of the Broca's area (see speech below).
8. ***Motor apraxia*** (inability to perform skilled movements by the hands in absence of paralysis due to damage of the hand skills area).

The following table shows the main causes of hypotonia and hypertonia

HYPERTONIA	HYPOTONIA
Lesion of area 6	Lesion of area 4
UMNL	LMNL
Parkinsonism	Chorea
Hemiballismus and athetosis	Neocerebellar syndrome
Decreased serum Ca^{++} level	Increased serum Ca^{++} level
Decerebrate animals	Tabes dorsalis
Neurotic and hysterical subjects	Peripheral neuritis
Certain congenital diseases	Myasthenia gravis

Functions of the supplementary motor area

1. It *supplements area 6* in providing attitudinal and fixation movements as a background for performance of fine movements.
2. It shares in *planning and programming* of complex voluntary movements

MECHANISM OF PERFORMANCE OF VOLUNTARY MOVEMENTS

The performance of voluntary movements requires the *motor and premotor cortex, cerebellum and basal ganglia, as well as the UMNs and LMNs*. They are carried out in 2 stages, ***planning then execution*** :

1. **Planning** : The idea of the movement originates in the ***cortical association areas*** from which signals are discharged to both the ***basal ganglia and the cerebrocerebellum***.

The basal ganglia convert thoughts into a motor plan and put the program of its performance, then discharges to the motor cortex (in which area 6 and the supplementary area share in the planning and programming processes).

On the other hand, the cerebrocerebellum also shares in the planning and programming processes and controls the discharge of signals from the motor cortex by its predictive and timing functions (for the proper performance of the sequential movements according to the plan).

2. **Execution** : The motor cortex discharges signals to the ***spinocerebellum as well as the spinal or cranial motor neurons*** (depending on the intended movement) via the UMNs (pyramidal tract). The former helps initiation of the movement and corrects any errors (by its servocomparator and damping functions) while the latter (LMNs) discharge to the skeletal muscles.

THE PARIETAL LOBE

This lobe contains the ***cortical sensory areas*** (so it is often called the ***sensory cortex***). These areas include the ***somatic sensory areas I and II, as well as the somatic sensory association area***.

The somatic sensory area I (areas 1, 2, 3)

This area is located at the ***postcentral gyrus***, and it receives sensations mainly from ***the opposite side***. In it, the body is represented in ***an inverted manner*** and the area of representation of any part is proportionate to the number of receptors it contains (and not to its size). It is concerned with

The following functions :

(a) Perception of fine tactile sensations and the senses of vibration, position and movements of joints

(b) Discrimination of weights and fine grades of temperature.

(c) Fine localization of various sensations.

Accordingly, **its damage leads to the following** :

(a) Inability to perceive the epicritic (fine) sensations from the opposite side.

(b) Crude localization of various sensations.

(c) Defects in motor performance (e.g. inability to execute learned sequences of movement).

The somatic sensory area II (area 40)

This area is located in the ***supramarginal gyrus*** behind the lower part of sensory area I. It receives signals from the latter area and potentiates its functions, and also starts *making meaning for the various sensory signals*. Its damage causes deficits in learning based on tactile discrimination.

The somatic sensory association areas (areas 5 & 7)

This area receives signals mainly from the somatic sensory areas, and is concerned with ***interpretation (= understanding) of various sensations*** (so it is also called the ***somatic interpretative area***). Its damage leads to failure of getting the meaning of sensations & ***astereognosis*** as well as ***amorphosynthesis*** (= forgetting the opposite side of the body).

THE OCCIPITAL LOBE

This lobe contains the ***visual centres (in areas 17, 18 and 19)***.

THE TEMPORAL LOBE

This lobe contains the ***auditory centres (in areas 22, 41 and 42)*** as well as an important ***association area*** (see next).

THE CORTICAL ASSOCIATION AREAS

(1) The prefrontal association area (areas 9. 10 & 11)

This area is concerned with the *high intellectual functions of the brain* and *elaboration of thoughts* as well as *planning the sequences of complex voluntary movements and the motor patterns for word expression*.

(2) The temporal (or limbic) association area (area 38)

This area is located mainly in ***the anterior pole of the temporal lobe***, and is concerned with *behaviour, emotions and motivation*.

(3) The parieto-occipito-temporal association area (areas 39&40)

This area occupies mainly ***the angular and supramarginl gyri in the parietal lobe***, and is concerned with the following :

a- ***Analysis of the spatial coordinates of the body and its surroundings***, so its damage causes ***amorphosynthesis*** i.e. failure of recognition of the contra-lateral side of the body (see above).

b- ***Language comprehension :*** This is performed by an importnt part of this area called ***Wernicke's area***, specially that in the ***dominant (= categorical) hemisphere*** (the *left one in 95 % of people*) where it is well developed. At this area, all interpretative areas meet (the somatic, visual and auditory interpretative areas) so it is also called the ***general interpretative area***.

c- ***Interpretation of visual language (reading) :*** This occurs in area 39 in the ***angular gyrus*** (see below).

d- *Naming of objects*.

SPEECH (LANGUAGE)

This is 2 types : ***spoken and written speech***, and each has 2 aspects :

1. **Sensory aspect** : This is the *understanding* of speech. It requires the integrity of the auditory and visual sensory and interpretative areas, as well as *Wernicke's area* (see below).
2. **Motor aspect** : This is the *process of vocaliztion itself*. It requires the integrity of the speech motor centre (Broca's area), the primary motor area (area 4), as well as the speech muscles and their innervation.

MECHANISM OF SPOKEN SPEECH

Spoken words are perceived at the *auditory sensory areas* (areas 41 and 42) and interpreted at the *auditory psychic area* (area 22). Signals are then discharged to ***Wernicke's area*** (in which full comprehension of the words occurs, the thoughts are determined and the expressing words are chosen). Signals from Wericke's area are then conveyed to *Broca's area* (area 44) via the *arcute fasciculus* which projects to area 4, and this discharges to the speech muscles in the lips, tongue, larynx, pharynx and respiratory system.

MECHANISM OF WRITTEN SPEECH

Written (or printed) words are perceived at the *visual sensory area* (area 17) and interpreted at the *visual psychic area* (area 18). From the latter, signals are then discharged to the ***angular gyrus*** (where early comprehension of the words occurs) which in turn discharges to ***Wernicke's area***. This area performs the functions described above, and from it, the sequence is the same as in case of spoken speech, resulting in ***reading***.

APHASIA (OR DYSPHASIA)

This is *abnormal speech*, and it is 3 main types (***sensory, motor & global***).

1. Sensory (receptive or fluent) aphasia

This is due to ***disorders in the sensory aspect of speech***, and it may be

a- **Auditory aphasia (word deafness)** : This is due to damage of the auditory psychic (or interpretative) area. The patient can hear spoken words, but he cannot understand their meaning. *So he can speak fluently, but his speech becomes a jargon (i.e. meaningless).*

b- **Visual aphasia (word blindness)** : This is due to damage of the visual psychic (or interpretative) area *or the angular gyrus*. The patient can see written words, but he cannot understand their meaning. *So on reading, he speaks fluently but his speech becomes meaningless.*

c- **Wernicke's aphasia** : This is due to damage of Wernicke's area. The patient can see, hear and understand words but he *cannot comprehend their ideas*. So he cannot formulate thoughts or put appropriate words, resulting in speech which may be fluent but meaningless.

2. Motor (expressive or nonfluent) aphasia

This is due to ***disorders in the motor aspect of speech***, mainly as a result of damage of Broca's area (so it is also called *Broca's or vocal aphasia*). The patient understands spoken & written words and knows what to be said and is able to vocalize, but his speech becomes slow and hard.

** Lesions of the hand skills area leads to a condition called **agraphia or writing aphasia**. This is *inability of the patient to write or draw* (when asked to) although he knows what to be done and can move his hands voluntarily for other purposes. It is believed to be due to damage of a special centre in this area called the ***writing (or Exner's) centre***. However, pure agraphia is rare, and it usually accompanies Broca's aphasia..

3. Global (general) aphasia

This occurs in *severe lesions of the dominant cerebral hemisphere*, and is due to damage of most speech centres. Both the sensory & motor aspects of speech are impaired, resulting in general aphasia in which the speech becomes ***hard and nonfluent***.

DYSARTHRIA

This is a speech abnormality due to *disorders in the act of articulation*. It occurs as a result of lesions in either the centres that control voluntary movements, the pyramidal and extrapyramidal tracts, or the lower motor neurons that supply the speech muscles, and the following are examples :

1. UMNLs lead to *spastic dysarthria* (stiff slurred speech).
2. LMNLs lead to *flaccid dysarthria* (nasal quality speech).
3. The neocerebellar syndrome leads to *staccato or scanning speech*.
4. Parkinsonism leads to *slow, monotonous and low volume speech*.

LEARNING

This is the process of acquiring knowledge and new responses. It is produced by 2 main ways, which are the following :

1. **Non-associative learning** : This is learning about a single stimulus e.g. by ***habituation and sensitization*** (page 18).
2. **Associative learning** : This is learning by pairing of stimuli, and the best example is learning by ***the conditioned reflexes*** (refer to Pavlov's experiment in GIT).

MEMORY

This is the ability of the brain to ***store and recall information***, and it is 2 main types :

1. **Reflexive (implicit) memory** : This is ***unconscious memory*** (e.g. the learned skills and the knowledge acquired by conditioning).
2. **Declarative (explicit) memory** : This is ***conscious recall of information***. It can be converted into reflexive memory by constant repetition, and it includes the following types :
    - (a) **Immediate (sensory) memory** : This lasts a few seconds then it either fades away or changes into one of the other types.
    - (b) **Primary (short-term or recent) memory** : This lasts a few minutes then it may or may not be consolidated (see below)..

(c) **Secondary (long-term or remote) memory** : This lasts for long times (up to several years).It develops from the previous types and is enhanced by ***rehearsal***. An advanced type in which the memory becomes permanent and rapidly recalled (e.g. one's name) is known as ***tertiary memory***.

Memory develops by ***strengthening of synaptic transmission***. In immediate memory, this is achieved by *post-tetanic synaptic potentiation and synaptic sensitization* (page 18) while in recent memory there is also *long-term potentiation as well as physical and chemical changes that increase synaptic transmission* On the other hand, in remote memory there is in addition, *structural (anatomical) changes in the presynaptic terminals*.

ENCODING OF MEMORY

In case of reflexive memory, encoding occurs in the *basal ganglia and cerebellum (where it is also stored)*. On the other hand, short-term memory is *temporarily stored in the prefrontal cortex*, then relayed to *the hippocampus and adjacent portions of the medial temporal cortex where it is processed and encoded*. Other areas are also involved in the encoding as well as the consolidation of short-term memories (see below), so patients with lesions of the hippocampus (or these other areas) retain old pre-lesion memories (both the implicit and explicit) and are capable of new learning but ***they cannot form new long-term memories***.

CONSOLIDATION OF MEMORY

Consolidation of memory means change of short-term memory into long-term memory. It requires integrity of the *prefrontal cortex, hippocampus, mamillary bodies of the hypothalamus, anterior thalamus, amygdaloid nuclei and the* ***neocortex*** (in which long-term memory is stored in many different parts and can be recalled by a large number of different associations).

Memory consolidation involves ***new synthesis of protein in neurons*** (so it is prevented by drugs or antibodies that block protein synthesis), and it becomes complete *after about 4 hours*. Short-term memories are also vulnerable (i.e. liable to be erased) during the first 5 minutes (i.e. while they are processed and encoded in the hippocampus) if disrupted by external stimuli (e.g. deep anaesthesia, electroshock therapy or brain concussion).

THE ELECTROENCEPHALOGRAM (EEG)

This is a record of the ***spontaneous brain electric activity in conscious subjects***. *4 types of waves are usually recorded*, which are the following :

1. **Alpha waves** (8-12 / second and voltage 50 microvolts). They are the dominant waves recorded in *conscious adults during rest*.
2. **Beta waves** (18-30 /second and lower voltage than alpha waves). They are recorded in *infants and during brain activity & increased tension in adults*.
3. **Theta waves** (4-7 / second and higher voltage than alpha waves). They are recorded in *children and during emotional stress and light sleep in adults*.
4. **Delta waves** (0.5- 4 / second and the highest voltage). They are recorded in *young infants and during deep sleep* (see below).

** EEG recording helps in *localization of focal lesions* (e.g. brain tumours and subdural haematomata) and *diagnosis of certain diseases* (e.g. epilepsy).

THE AROUSAL OR ALERTING RESPONSE

This is an EEG response that occurs when the subject becomes alert e.g. when he opens his eyes or solves a mathematical problem. The synchronized alpha rhythm is replaced by a *rapid low voltage beta rhythm*, so the response is also called ***alpha block or desynchronization***. It is due to stimulation of the ***ARAS*** (see below), and is ***reversible*** (i.e. the alpha rhythm is resumed after stoppage of the brain activity).

PHYSIOLOGY OF CONSCIOUSNESS

Consciousness and wakefulness are the result of ***generalized excitation of the cerebral cortex***, which is the function of a part of the reticular formation called the ***ascending reticular activating system*** (see below).

The reticular formation (RF)

The RF is a network of neurons located in the brain stem. It contains several centres and nuclei within its meshes, and it consists of 2 main parts :

1- **A sensory part** : This receives *afferent fibres* from almost all parts of the nervous system.

2- **A motor part** : This gives *efferent fibres* from the RF, and is divided into 2 parts, which are the following :

a- **Facilitatory RF** : This has *an ascending branch* (= ARAS) which activates the cerebral cortex, and *a descending branch* (= the ventral reticulospinal tract) which facilitates the spinal motor neurons (page 30).

b- **Inhibitory RF** : This forms the lateral reticulospinal tract which inhibits the spinal motor neurons (page 31).

The ascending reticular activating system (= ARAS or RAS).

This is a *multineuronal polysynaptic system of nerve fibres* that originates at *the facilitatory RF*. Its fibres extend upwards to the *thalamus*, where most of them relay at its *nonspecific nuclei*, then other fibres arise and project *diffusely to almost all parts of the cerebral cortex (= reticulo-thalamo-cortical pathway)*. ***The ARAS increases the electric activity of the cerebral cortex*** and is concerned with production of ***consciousness as well as the arousal response*** (see above).

The factors that *increase* the ARAS activity include **(a)** Signals from the sensory pathways(specially pain) and the cerebral cortex (via corticofugal fibres e.g. during emotions) **(b)** Analeptic drugs e.g. amphetamine & caffeine. On the other hand, the ARAS activity is *decreased* if it is damaged (e.g. by tumours) or the signals to it are reduced, as well as by the anaesthetic drugs.

SLEEP

Sleep is a physiological state of temporary unconsciousness. It is **2 types** :

1. **Slow wave sleep (non-REM sleep)** : This type passes in *4 stages* :
   - a- ***Stage 1*** (EEG shows theta wave rhythm).
   - b- ***Stage 2*** (EEG as stage 1 + alpha like waves called *sleep spindles*).
   - c- ***Stage 3*** (EEG shows *delta waves* at a frequency of 3 - 4 / sec).
   - d- ***Stage 4*** (EEG shows *delta waves* at a frequency of 0.5-1.5 / sec).
2. **Rapid eye movement sleep (REM or paradoxical sleep)** : This follows the slow wave sleep and the EEG shows ***desynchronized beta rhythm*** (like the arousal response). During it, *dreams, bruxism and penile erection* occur.

The sleep cycles : Sleep normally starts by the slow wave type (4 stages) for about 90 minutes then REM sleep follows for about 20 minutes, and this is repeated cyclically over the period of sleep (e.g. during a night's sleep).

MECHANISM (THEORIES) OF SLEEP

Sleep occurs after a period of wakefulness as a result of depression of the cerebral cortex ***secondary to inhibition of the ARAS***. Such inhibition occurs by one (or both) of the following 2 mechanisms :

1. **Passive mechanism** : This assumes that the *ARAS activity is decreased* as a result of its fatigue.
2. **Active mechanism** : This assumes that the *ARAS activity is decreased* by signals discharged from the following ***2 sleep centres*** :
   - a- *A centre in the raphe nuclei* : This releases *serotonin*, and induces slow wave sleep (so serotonin is sometimes called the ***sleep hormone***)
   - b- *A centre in the RF at the upper brain stem* : This induces REM sleep.

** It is also claimed that sleep is induced by *certain sleep imducing factors*, and that *serotonin induces sleep by promoting synthesis of these factors.*

MECHANISM OF THE SLEEP / WAKEFULNESS CYCLE

Activation of the ARAS leads to wakefulness through excitation of the cerebral cortex by signals discharged via the ***reticulo-thalamo-cortical pathway*** (see above). This state is then *maintained* by a ***+ve feedback mechanism*** through re-excitation of the ARAS by signals discharged from the activated cortex to the RF via the ***corticofugal fibres*** (which constitute a ***cortico-thalamo-reticular pathway***).

After wakefulness continues for some time, sleep occurs due to either fading away of the +ve feedback cycle (as a result of fatigue of the ARAS) or spontaneous activation of the sleep centres. Then, during the sleeping hours, the ARAS gradually recovers its activity (and the sleep centres also become less excitable), so it discharges excitatory signals to the cerebral cortex, leading to wakefulness, and a new cycle begins.

The following table compares slow wave (non-REM) and REM sleep :

	SLOW WAVE SLEEP	REM SLEEP
Occurrence	At the start of sleep (4 stages)	After the slow wave sleep
Duration / cycle	About 90 minutes	About 20 minutes
Duration / a night's sleep	75 - 80 %	20 - 25 %
Eye movements	The eyes deviate up + miosis	Rapid roving movements
Centre	In the raphe nuclei	In RF at upper brain stem
Talking and walking	Present	Absent
Dreams, bruxism, erection	Absent	Present
Heart & resp. rates & ABI	Usually decrease	Usually increase
Muscle tone	Decreases slightly	Decreases markedly
Depth of sleep	Increases gradually with stage	Light
EEG pattern	Differs with the stage (see text)	desynchronized beta rhythm
Arousal (awakening)	Slow (and at a high threshold)	Fast (at a relatively high th

POSTURE AND EQUILIBRIUM

The reflexes that regulate posture and equilibrium are initiated at the *proprioceptors, visual receptors & the non-auditory labyrinth* (= *vestibular apparatus*) which consists of the ***utricles, saccules and the semicircular canals***.

THE UTRICLES AND SACCULES

These are sacs that contain *endolymph* and mechanoreceptors called ***maculae or otolith organs***. Each macula is formed of a ridge of supporting & hair cells covered by a gelatinous layer in which the cilia of the hair cells project and *crystals of Ca carbonate **(called otoliths or otoconia)*** are embedded. They are stimulated by the ***effect of gravity***. This moves the otoliths, so the cilia bend (which excites the hair cells, leading to discharge of signals in the vestibular nerve).The utricles and saccules perform the **following functions**:

1. They detect **(a)** changes in *the position of head* **(b)** *linear acceleration*.
2. They *initiate many postural reflexes* (see below).

THE SEMICIRCULAR CANALS (SC)

There are 3 SCs on each side (*horizontal, anterovertical & posterovertical*) arranged at right angles (representing the 3 planes of space). Each SC contains endolymph and a mechanoreceptor called ***crista ampullaris***. Each crista is formed of a ridge of supporting and hair cells the cilia of which project into a large gelatinous mass called ***the cupula***. They are stimulated by ***bending of the cilia as a result of deflection of the cupulae to either side***.

** Each hair cell has 50-70 small movable cilia called ***stereocilia***, and one large stiff cilium called the ***kinocilium***. In case of *the horizontal canals*, the kinocilia are located *towards the utricles, and when the stereocilia bend towards the kinocilia (i.e. towards the utricles), the hair cells are stimulated* and vice versa. The opposite is true in the vertical canals.

The only function of the SCs is ***detection of angular acceleration and initiating the appropriate reflexes*** that maintan equilibrium (but they are *insensitive to angular movements of constant velocities*). In addition, on stimulation, ***they produce other effects***, which can be studied as follows :

Methods of stimulation of the SCs

1. ***Electric stimulation*** (by electrodes placed on the ***mastoid process***).
2. ***Caloric stimulation*** (by ***cold or hot water instilled in the external ear***).
3. ***Mechanical stimulation*** (by rotating the subject in a ***revolving chair***).

In the last method, if the subject was rotated from ***left to right in the horizontal plane***, the ***inertia of the endolymph*** causes its lag, so it flows in the opposite direction, resulting in deflection of the cupulae of the horizontal canals to the left. Thus the right crista is stimulated while the left crista is inhibited (see above). Such unbalanced discharge from the 2 sides gives a sensation of rotation to the right and also produces other effects (see below).

As rotation continues, the inertia of the endolymph is overcome so the cristae return to the resting position and the sensation of rotation disappears. However, after rotation stops, the endolymph moves ***by its momentum*** in the direction of rotation, resulting in deflection of the cupulae to the right. Thus the left crista is stimulated while the right crista is inhibited, resulting in a sensation of rotation in the opposite direction (i.e. to the left) called ***vertigo***, in addition to ***post-rotatory nystagmus and other effects*** (see below).

Effects of stimulation of the SCs

These effects are produced by signals discharged from the stimulated crista. In addition to the sensation of *angular acceleration* (perceived at the equilibrium centre in the superior temporal gyrus), the following also occur

(1) Nystagmus : This is a jerky to and fro movement of the eyes. It occurs *at the start of rotation and after it stops (but not during constant rotation).* and it consists of ***2 components***. The rotatory nystagmus shows a slow movement in an opposite direction to that of rotation followed by a fast movement in the same direction, and it ***helps maintaining a stable image on the retina***.On the other hand, the directions of the 2 components of post-rotatory nystagmus are ***reversed*** because the other crista is stimulated due to movement of the endolymph by its momentum, and ***it exerts no function***.

Nystagmus occurs by a ***vestibulo-ocular reflex***. It is initiated by signals from the cristae (*not by visual impulses*) to the vestibular nucleus then to the ***medial longitudinal bundles at both sides***, which control the nuclei of the cranial nerves that innervate the ocular muscles (3rd, 4th & 6th cranial nerves)

(2) Vertigo : This is a ***false sensation of counter-rotation*** (i.e. rotation in the opposite direction) that is felt for about 20 seconds after rotation stops.

It is due to stimulation of the other crista caused by movement of the endolymph by its momentum (see above). Signals from the crista are conveyed to the *equilibrium centre in the superior temporal gyrus of the opposite side* (where the sensation is perceived) via ***a vestibulo – cerebello – thalamo - cortical and a vestibulo – reticulo – thalamo - cortical pathways***.

(3) **Past pointing effect of Barany** : This occurs as a compensatory reaction to the sensation of vertigo. If the subject ***with closed eyes*** is asked to touch a certain point, his finger deviates to the direction opposite to that of vertigo i.e. in the direction of original rotation(also the direction of falling if occurs)

(4) **Autonomic effects** : Several autonomic effects occur after rotation due to excitation of the autonomic centres in the reticular formation by signals discharged from the stimulated crista (e.g. *bradycardia and hypotension, sweating, pallor, increased respiratory rate and nausea and vomiting*).

(5) **Changes in muscle tone** : The tone increases in the muscles at the same direction of rotation and decreases in the opposite side. This helps maintenance of posture and equilibrium, and is conveyed by signals discharged to the spinal motor neurons via *the vestibulospinal and reticulospinal tracts*.

Meniere's syndrome : This is a disease due to rise of pressure of the endolymph in the SCs, and is characterized by severe attacks of vertigo, nystagmus and vomiting.

THE POSTURL REFLEXES

These are usually classified into *static and statokinetic reflexes*.

(I) STATIC POSTURAL REFLEXES

(1) **Local static reflexes** : These involve *one limb*, and include ***the stretch reflex*** (page 25) and the ***positive supporting reaction*** (pages 21 and 22).
(2) **Segmental static reflexes** : These involve *2 limbs*, and include the ***crossed extensor reflex*** (page 24) and ***Philipson's reflex*** (page 30).
(3) **General static reflexes** : These include ***statotonic and righting reflexes***.

(A) Statotonic reflexes : These are ***2 types*** :

1. **Statotonic neck reflexes** :
a- Dorsiflexion of head → extension of forelimbs & flexion of hind limbs
b- Ventroflexion of head → flexion of forelimbs & extension of hind limbs
c- Head rotation → extension of ipsilateral limbs & flexion of opposite limbs

The receptors of these reflexes are the *neck proprioceptors* and the afferent fibres are the *upper 3 cervical nerves*. Their centre is the *vestibular nucleus* and the efferent fibres are the *vestibulospinal and reticulospinal tracts*.

2. Statotonic labyrinthine reflexes :

a- Placing the animal in the supine position → extension of the 4 limbs.

b- Placing the animal in the prone position → flexion of the 4 limbs.

The receptors of these reflexes are the *otolith organs* and the afferent fibres are the *vestibular nerves*. Their centre is the *vestibular nucleus* and the efferent fibres are the *vestibulospinal and reticulospinal tracts*.

(B) Righting reflexes (RRs)

These restore the standing position if it is disturbed, and are initiated by signals discharged from the *otolith organs, neck proprioceptors, pressure receptors of the body as well as the visual receptors*. They include the following reflexes (the centre of the first 4 reflexes is the ***mid brain***) :

1. *Labyrinthine RR on the head.* **2.** *Body RR on the head.*
3. *Neck RR on the body.* **4.** *Body RR on the body.*
5. *Visual (and voluntary) RR* (centre is the ***cerebral cortex***).

The grasp reflex

The hand of a thalamic (decorticate) animal grasps an object firmly and resists its pull out. It is considered a ***supporting reaction*** and is ***normally present in newly-born infants***. However, it disappears in adults with development of the frontal lobe, so lesions of this lobe, specially area 6, are associated with reappearance of this reflex (page 53).

(II) STATOKINETIC POSTURAL REFLEXES

These reflexes *maintain equilibrium during movement*, and include :

1. **Linear acceleration reflexes** (acceleration causes reflex leaning forwards while deceleration causes reflex leaning backwards).
2. **Angular acceleration reflexes** (extension of the limbs in the same direction of rotation, and flexion of the limbs in the opposite side).
3. **Cortical statokinetic reflexes** : These include the following reflexes :
   - **a-** *The hopping (jumping) reflex.*
   - **b-** *The placing reflexes (contact and chin placing).*
   - **c-** *The dynamic visual reflexes.*

UNIVERSITY BOOK CENTRE

8 Soliman EL Halaby Str., Cairo

Tel. 5774881 - 3957807

Fax: 5897635 - Mobile 0123698600